# THE
# PRACTICE *of* MEDICINE

*By*

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SIR WILLIAM OSLER, BT., M.D., F.R.S.

MEDICAL PHILOSOPHER, MASTER CLINICIAN, TRUSTED COUNSELOR

THIS BOOK IS GRATEFULLY DEDICATED

BY

HIS ONE-TIME PUPIL

# PREFACE

THE object I have endeavored to attain in the preparation of this work is to present descriptions of the various internal diseases which should accord with the present state of our knowledge, and, which, though concise, should give to the student and practicing physician the most necessary points in pathology, diagnosis and treatment. In order to keep the material within reasonable limits I have omitted clinical records of my own and of others which would have served as illustrations of the text, and for the same reason, I have disregarded, for the most part, all controversial questions and all theories still under discussion. Nevertheless I have tried to indicate what seem to be the important issues of the day and to point out that many conclusions which are generally accepted as final are in reality only provisional and with more accurate observation and more critical consideration of results may have to be greatly modified. I have not the ability, nor have I attempted, to supply all the information that the internist needs, but I have consulted the writings of many authorities, both American and foreign, and have supplemented the information obtained from these sources by what I have learned myself in thirty years of practice in various hospitals and elsewhere, as well as of teaching, first in pathology and then in internal medicine, and I venture to hope that nothing of real importance has been omitted, and that the book will be found a trustworthy guide to the practice of Medicine.

Certain references have been inserted in the book for the benefit of those who may wish to study more fully any particular subject. Those selected are to contributions which themselves present a more or less complete bibliography, which deal with comparatively recent investigations, which are of exceptional importance, or which are historically interesting.

Finally, it is with much pleasure that I acknowledge my obligation to Dr. Thomas M. McMillan, of the medical staff of the Philadelphia General Hospital, for the preparation of the excellent electrocardiographic records.

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# CONTENTS

## INFECTIOUS DISEASES

## INTOXICATIONS



## FOOD DEFICIENCY DISEASES



## DISORDERS OF METABOLISM



## DISEASES OF THE DIGESTIVE SYSTEM

## DISEASES OF THE RESPIRATORY TRACT



## DISEASES OF THE CIRCULATORY SYSTEM

## DISEASES OF THE KIDNEYS

## INDEPENDENT DISEASES OF THE BLOOD-FORMING ORGANS AND THE ANEMIAS



## THE HEMORRHAGIC DISEASES



## DISEASES OF THE SPLEEN

## DISEASES OF THE DUCTLESS GLANDS



## DISEASES OF THE JOINTS AND BONES



## DISEASES OF THE MUSCLES AND MYOPATHIES WITHOUT OBVIOUS CHANGES IN THE NERVOUS SYSTEM



## DISEASES OF THE NERVOUS SYSTEM

## DISORDERS DUE TO EXCESSIVE HEAT



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# INFECTIOUS DISEASES

## INFECTIONS DUE TO BACTERIA

### TUBERCULOSIS

**Definition.**—A specific, infectious and mildly contagious disease, communicable directly from host to host, caused by Bacillus tuberculosis, and characterized in its most typical form by the appearance of small circumscribed nodules of granulation tissue, or tubercles, which tend to undergo caseation and softening, but which under favorable conditions may become calcified or be transformed into fibrous tissue. The lesions may be widespread, as in acute general tuberculosis, but usually at first they are limited to one organ or tissue, as in tuberculosis of the lungs.

**History.**—Tuberculosis has existed from the most ancient times. Hippocrates (406–377 B.C.) described very accurately the clinical manifestations of the pulmonary tuberculosis, or phthisis, but thought that it was caused by the secretions of the head flowing into the bronchi. Belief in the contagiousness of the disease seems to have been general among the Greek contemporaries of Hippocrates. Sylvius (1695) was the first to associate tuberculous nodules with phthisis, although he regarded them as enlarged lymph nodes. In the latter part of the eighteenth century Stark gave an accurate description of tubercles and in the early part of the nineteenth century Bayle showed that tuberculosis was a constitutional condition that could cause the appearance of tubercles in all the organs. To Laënnec belongs the credit of recognizing that all forms of pulmonary consumption or phthisis are tuberculous and of advocating the identity of so-called scrofula and tuberculosis of the lymph nodes. Laënnec's teachings, however, were not generally accepted and even Virchow for a time thought that phthisis and tuberculosis were different diseases. This error was finally overthrown by the discoveries of Villemin and Koch. Villemin in an extensive series of experiments conducted between 1865 and 1869, not only confirmed the observation originally made by Klencke (1843) that tuberculosis is transmissible by inoculation, but also clearly demonstrated the specific infectious nature of the disease. He concluded that the inoculation of tubercle does not act through any pathologic product that enters with it, but "through a more subtle agent which is contained in it, and which escapes our perception." The "subtle agent" was detected and isolated as the tubercle bacillus by Koch in 1882.

**Etiology.**—Tuberculosis occurs in all parts of the world and it affects not only human beings but also many of the lower animals, especially cattle and birds. So far as mankind is concerned no *race* is immune to it, although it is preeminently a disease of *civilization*. It is estimated that the civilized world loses by death from tuberculosis nearly 1,000,000 individuals annually, and it is not improbable that in large cities almost every person has received some tuberculous infection by the time he reaches puberty (Naegeli, Hamburger, Baldwin). In the United States the annual mortality from tuberculosis is now about 100,000, which is more than from any other illness except heart disease and pneumonia. From 1881 to 1917, however, the death-rate from tuberculosis in all its forms fell from about

390 to 146 per hundred thousand. This decrease in mortality is doubtless due in large part to better sanitation, a clearer understanding by the public of what predisposes to the disease, and to improved methods of treatment, but it may be due in part also to the gradual inheritance of an acquired immunity or to the gradual elimination of the most susceptible subjects, for it is well known that when tuberculosis attacks populations that for centuries have been unexposed to it, epidemics of great virulence ensue.

*Heredity.*—While it is possible, but not proved, that persons who recover from tuberculosis may transmit a certain resistant quality to their offspring and that in consequence a gradual process of immunization is taking place in civilized communities, there is no reason to believe that parents with active tuberculosis transmit any unusual resistance to their children. Indeed statistics seem to show that persons with a pronounced family history of tuberculosis are somewhat more disposed to the disease than others. Inherited predisposition, however, is undoubtedly much less important than was formerly believed, the greater prevalence of tuberculosis among the offspring of tuberculous parents being due mainly to a greater chance of direct contagion. If a child born of a phthisical mother is at once removed from the danger of contagion it usually grows up without developing the disease.

*Age.*—Since the time of Hippocrates it has been recognized that early adult life is the period in which tuberculosis most frequently becomes manifest clinically and that the greatest number of deaths occur between the ages of 15 and 40. Nevertheless, postmortem examinations of children who have died of various diseases and the evidence obtained experimentally with specific tests strongly support the view advanced especially by von Behring that primary tuberculous infection occurs usually in infancy or childhood, but in the large majority of cases is either successfully combated or only develops when the individual reaches adult life. Evidence of tuberculosis is not often found in infants less than six months old, but from this age up to puberty the incidence rapidly increases. In rare instances, however, tuberculosis is congenital being transmitted by a mother in the advanced stages of the disease by way of the placenta. Whether the tuberculosis of adults arises more frequently from the lighting up of a latent focus acquired in childhood or from a new infection from without is not definitely known, but the evidence favors the view that autogenous infection is the rule and adults are often unharmed by contact with the bacillus owing to a relative immunity that has resulted from earlier slight infections.

*Lessened Resistance.*—By reducing the resistance of the individual certain conditions predispose to infection, or if infection has already occurred and is latent tend to develop it into active tuberculosis. Foremost among these conditions are unsanitary surroundings, underfeeding, vicious personal habits, abuse of alcohol, occupations that involve the inhalation of dust or any irritative particles, and certain other diseases, especially recurrent catarrh of the respiratory tract, measles, whooping cough, diabetes, cirrhosis of the liver and stenosis of the orifice of the pulmonary artery. Bronchopneumonia of adults and serous pleurisy are often followed by active pulmonary tuberculosis, but chiefly because these diseases are in many instances of tuberculous origin. So, too, the conformation of the chest known as the phthisical habitus (long flat chest with slanting ribs and prominent scapulæ) is probably a result of early infection rather than a sign of predisposition. Whether or not pregnancy in healthy women increases susceptibility to infection is not definitely known, but that latent or quiescent tuberculosis is very often rendered active by pregnancy is generally con-

ceded. It is doubtful whether traumatism ever actually originates the disease, but, as is well known, it may aggravate or render manifest a tuberculous lesion previously existing either at the site of the injury or in some other part of the body, and by setting free great numbers of bacilli from a sequestered focus it may also give rise to disseminated miliary tuberculosis.

The fact must not be overlooked that even without any special predisposition a normal resistance may be overcome by massive or continuous infection with virulent microörganisms.

*Climate* in itself does not appear to be an important factor in the etiology of tuberculosis, but cold and dampness by favoring indoor life and predisposing to catarrhal conditions may increase the liability to infection. The chances of infection are increased by *density of population*, and therefore the disease prevails more extensively in cities than in the country. The poor, owing to overcrowding and insufficient food and clothing, suffer in greater proportion than the rich.

**The Bacillus.**—The bacillus of tuberculosis is an aërobic, non-motile straight or slightly curved rod, with rounded ends and frequently a beaded appearance. It grows slowly upon suitable media and multiplies by fission, but it does not propagate outside the body under ordinary conditions, its life being wholly parasitic. It can, however, retain its vitality in sputum, on fabrics, and in dust for weeks, although probably the larger number soon die. It is readily killed by many chemical agents and by boiling, and apparently it succumbs in a few days to the action of direct sunlight. While somewhat widely distributed, it is not ubiquitous as are the common pyogenic organisms. Owing to the presence of a fat-like substance within its protoplasm the tubercle bacillus is resistant to acids and alcohol after coloration with certain anilin dyes, and in this respect it resembles the bacillus of leprosy and the smegma, grass, and butter bacilli. The organism may be readily demonstrated in sputa and other pathologic fluids by the Ziehl-Neelsen method or better still by this method after the material has been heated with antiformin,[1] which dissolves pus, mucus, and all other bacteria.

Koch in his attempts to influence the course of tuberculosis through active immunization, prepared a concentrated filtrate of a glycerin-broth extract of the bacilli, which he called *tuberculin*. A small dose of this substance when injected into an animal free from tuberculosis has little or no effect, but when injected into an infected animal it produces fever and a marked inflammatory reaction at the site of the disease. These phenomena seem to be due to a peculiar nuclein, which is set free from the dead bacillus and which probably constitutes its chief endotoxin. There is no evidence that any toxin is actively secreted by the living bacillus. In susceptible animals dead bacilli produce tubercles indistinguishable from those caused by living bacilli. The bacilli of human and bovine tuberculosis, while closely related, are not identical, and there is no proof that transmutation of the one type into the other ever occurs. Cattle are to a considerable extent immune from the bacillus of human tuberculosis, but human beings are more or less susceptible to the bovine bacillus. So far as adult human beings are concerned the bovine bacillus seems to be a negligible factor. Only a very few cases of pulmonary tuberculosis with this type of bacillus in the sputum have been reported. In children, however, a certain percentage of tuberculous infections elsewhere than in the lungs, as in the abdominal lymph nodes, bones and joints is found associated with the bovine bacillus, trans-

[1] Antiformin is a 10 per cent. solution of sodium hypochlorite containing 5 to 10 per cent. of sodium hydrate.

mission being through the milk and by way of the intestine. The avian, piscine and reptilian types of the bacillus play no part in human pathology.

**Sources of the Bacilli and Modes of Infection.**—It is the consensus of opinion that the *sputum* of patients with pulmonary tuberculosis is the chief source of infection and that the *inhalation* of tubercle bacilli is the most frequent cause of the disease, especially in adults. The bacilli may be contained in the dust of dried sputum or in the minute droplets of sputum or mucus that are ejected in coughing, sneezing, etc. Droplet infection is only operative, of course, under circumstances of close intimacy. The bacilli may lodge in the smaller bronchi and produce a tuberculous bronchitis or they may invade the alveoli and set up a primary pulmonary tuberculosis. Less frequently, after gaining access to the mouth, they appear to reach the cervical lymph nodes and distant organs through the *tonsils or fauces*.

*Ingestion* is next in importance to inhalation as a mode of infection. Bovine tuberculosis is not rarely transmitted to young children through the milk of infected cows, especially cows with disease of the udder. Butter made of milk containing the bacilli may also be infective. Food of various kinds may be contaminated by being incautiously handled by tuberculous subjects. The meat of tuberculous animals is probably not an important factor as it is usually sterilized by cooking. Bacilli carried into the alimentary canal with foodstuffs may reach the cervical lymph-nodes or the tracheobronchial lymph-nodes through the tonsils or the pharynx, or perhaps in some instances through cavities in the teeth. In the majority of cases, however, bacilli derived from food enter the intestine. Infection through the stomach is rare. Enterogenic infection may give rise to primary tuberculosis of the intestine, but this is exceptional; usually the bacilli pass through the wall of the bowel without producing any lesion, and reach the mesenteric lymph-nodes or the thoracic duct, whence they may invade the lung or other distant organs.

Infection through the *inoculation of a wound* is relatively unimportant, but it is sometimes acquired by pathologists in making postmortem examinations on tuberculous subjects and by butchers and others in handling tuberculous carcasses. Exceptionally it has resulted also from contact with a sharp fragment of a broken spittoon (Merklen, Lesser, Holst), from the bite of a consumptive (Vercheré, Jeanselme), from ritual circumcision (Ware, Reuben), from skin-grafting (Czerny), from tattooing (Jadasohn), or from a hypodermic injection (Bruns). In such cases the infection usually remains more or less local and takes the form of a tuberculous wart; rarely, however, it may cause secondary involvement of the lymph-nodes and pulmonary or other widespread tuberculosis.

*Prenatal transmission* is rare. When it does occur it usually takes place through the placenta. Proof of germinal infection through the spermatozoön or ovum is not conclusive, although the possibility must be admitted.

**Paths of Dissemination.**—Having entered the body the bacilli may be disseminated in various ways: (1) By growth through the tissues. In this way the margin of a single focus is gradually extended and groups of tubercles are formed into conglomerate masses. (2) By the lymphatics. This is one of the commonest modes of dissemination, especially in the subacute and chronic forms of the disease. (3) By natural passages. Thus, in pulmonary tuberculosis bacillus-laden sputum may be aspirated from one bronchus into another and so cause new areas of disease or the sputum may be swallowed and infect the intestine. Again, the lower urinary tract may be infected from the kidney by way of the ureter. (4) By the bloodvessels. A caseous tuberculous lymph-node sometimes ruptures into a vein, or, less frequently,

into an artery and thus the bacilli are carried to distant parts. From a pulmonary vein they are distributed all over the body, from a systemic vein they are conveyed to the lungs, and from an artery they are transported to the area supplied by the invaded vessel. The sudden introduction of a great number of bacilli into the blood stream is followed by an eruption of numerous tubercles in various organs. Such a condition is known as general miliary tuberculosis.

**Morbid Anatomy.**—Having entered the tissues tubercle bacilli may die before they can do any harm, or they may remain latent until some accident determines their active growth, but if at the time, the resistance of the tissue is weak, or what is equivalent, the bacilli are especially virulent, then characteristic changes are at once produced. The most frequent change is the appearance of minute spherical masses of newly formed cells which are called *tubercles*. Each tubercle is composed, as a rule, of three cellular elements—a central giant cell with numerous marginal nuclei, a middle layer of large ovoid or polygonal cells with elongated vesicular nuclei (epithelioid cells) and an outer layer of lymphoid cells. A supporting reticulum may also be present. Bacilli are usually found within the giant cells and between the epithelioid cells. None of these elements, with the exception of the bacilli, is peculiar to tuberculosis, but the arrangement of the cells is fairly distinctive. The origin of the various cells in the tubercle is still under discussion, but the weight of evidence favors the view that the epithelioid cells are derived from local endothelial and connective tissue cells, that the giant cells arise from fusion of adjacent epithelioid cells or from single epithelioid cells in which there has been division of the nucleus without division of the protoplasm, and that the lymphoid cells are lymphocytes from the surrounding vascular and lymphatic channels, the chemotactic influence of the tubercle bacillus or its products being lymphocytic rather than polynuclear leucocytic. Single tubercles are microscopic but usually a number develop coincidently and become confluent, forming the so-called *miliary tubercle,* which is about the size of a millet seed. When very young the miliary tubercle is gray and translucent, but in a short time it becomes yellow or white and opaque, owing to necrosis and caseation. These regressive changes are due in part to the lack of capillaries in the tubercle and in part to the action of the specific products of the tubercle bacillus. The affected cells lose their power of staining and become more homogeneous, and finally break up into granular detritus.

The escape of bacilli from the disintegrating tubercle into adjacent lymph spaces is followed by the formation of fresh tubercles, which in turn undergo caseation, and thus a large conglomerate mass of tubercles, with a central cheesy aera, may eventually be developed. Later, such a mass may undergo liquefaction (often because of a secondary infection by pyogenic organisms) and evacuate itself externally, leaving behind a cavity or an ulcer; or, under favorable conditions, it may, like any other foreign body, become surrounded by a dense, contracting fibrous capsule and ultimately be transformed through the deposition of lime-salts into a gritty or stony nodule. As a rule, the bacilli remain alive, with power to renew the infection so long as the cheesy material persists; occasionally, however, they die, and in this event, the tubercle, if small, may undergo complete absorption.

In contrast with the circumscribed nodules just described, but often associated with them, the tubercle bacillus sometimes causes diffuse inflammatory processes of various kinds. Thus, a *diffuse granulation tissue* may be produced, especially if a great number of bacilli exert their influence at the same time over a large extent of tissue, as in the lymph-nodes, kidney and

testicle, and on serous surfaces. This tuberculous granulation tissue, unlike the tubercle, presents numerous newly-formed bloodvessels, and is distinguished from the granulation tissue of simple inflammation by the sparsity of polymorphonuclear leucocytes, by the presence of epithelioid cells and, perhaps, giant cells, and also by a strong tendency to undergo necrosis and caseation.

Again, the reaction of the tissues to invasion by the tubercle bacillus may consist chiefly in the formation of a serous, fibrinous or purulent exudate. This *exudative form of tuberculous inflammation* occurs especially in the meninges, in serous cavities, and in the lungs. The exudate is similar to that produced by ordinary inflammation, but differs in the presence of the specific organisms, the preponderance of lymphocytes over polymorphonuclear leucocytes, and not rarely in the appearance of characteristic tubercles or tuberculous granulation tissue. In the lung tuberculous exudative inflammation is well exemplified by caseous tuberculous pneumonia. In this condition exudative products fill the alveoli, as in croupous pneumonia, but instead of dissolving or becoming organized in the usual way, they rapidly undergo cheesy necrosis.

Finally, the evolution of the tuberculous process may be characterized by the *production of a large amount of fibrous tissue.* This fibroid change is brought about by the transformation of the epithelioid cells of the tubercle, which are genetically fibroblasts, into fibrous connective tissue and occurs especially when the virulence of the bacilli is low or the resistance of the subject is high. Ordinarily, the toxic action of the bacilli is strong enough to kill the epithelioid cells before they have had time to develop into connective tissue. Once begun, fibrosis may progress, if the conditions are favorable, until the tuberculous focus is surrounded and sequestered or is completely absorbed. In some cases the tubercle shows a tendency from the first to make scar tissue, necrosis or caseation being slight or absent, and therefore it is conceivable, as French writers have urged, that the tubercle bacillus may produce both a fibrogenic and a caseogenic endotoxin.

**Sites of Tuberculosis.**—As most persons offer considerable resistance to infection by the tubercle bacillus, the tuberculous process, irrespective of the avenue of invasion, usually remains more or less localized. Some of the tissues are apparently less sensitive to the bacillus than others. The upper respiratory and alimentary tracts, for instance, although often serving as portals of entry, have themselves little tendency to the disease. The skin is also relatively immune, and when it is invaded the lesions usually remain localized and tend to heal. Of all the organs, the lungs show the greatest disposition to tubercle formation. Next to the lungs, the lymph-nodes, joints, bones and serous membranes are the most frequent points of attack.

**Tuberculin Tests in Diagnosis.**—When there is some doubt as to whether tuberculosis is present or not, additional evidence may often be obtained from the tuberculin tests, the basis of which is the peculiar (allergic) reaction that is excited in an infected subject by the parenteral reintroduction of the specific poison (antigen) corresponding to the infection. Unfortunately in the case of tuberculosis positive reactions may occur even if the focus of disease is latent or quiescent. Negative reactions, however, point strongly to the entire absence of tuberculosis. The *subcutaneous* test with Koch's old tuberculin is the most reliable, although it is not entirely free from the danger of aggravating any existing infection and its results are difficult of interpretation unless the patient is apyretic. The test is made by injecting below the angle of the scapula from 0.1 to 1.0 milligram of tuberculin, according to the state of the patient's health, and then taking the temperature

at short intervals. In the absence of any rise of temperature the dose may be increased 0.5 or 1.0 milligram every two or three days until 5 or even 10 milligrams are given. If the reaction is positive the injection is followed in from 6 to 16 hours by an increase of 1 to 3 degrees (F.) in the temperature, with chilliness, headache and general malaise and an inflammatory reaction (redness and swelling) at the point of injection. Even more significant is evidence of increased activity at the seat of disease, shown in the case of pulmonary tuberculosis by a more abundant expectoration and more pronounced physical signs. The test should not be made if laryngeal tuberculosis is suspected, or if nephritis, diabetes, cardiac disease or pregnancy is present.

The *cutaneous tests of von Pirquet and Moro* cause only local reaction at the point of inoculation and are usually positive in tuberculous patients unless the disease is far advanced. Neither test, however, serves to distinguish between an active and an inactive process and neither is reliable after the second or third year, as a large percentage of older persons have already been infected sufficiently to yield positive reactions. In von Pirquet's test the arm having been thoroughly cleaned, a drop of old tuberculin is placed on the skin at two points about 10 cm. apart. A spot midway between the two drops is now scarified with a special instrument until slight oozing of serum occurs and then similar scarifications are made directly through each of the tuberculin drops. After the parts have become dry they may be protected by a handkerchief. If the reaction is positive a red papule, surrounded by an inflammatory areola, appears in from 12 to 24 hours at each of the two test points. Moro's test consists of rubbing into the skin of the abdomen (an area 5 cm. in diameter) for about a minute an ointment (0.5 gm.), composed of equal parts of the old tuberculin and lanolin. A positive reaction is shown by the appearance of general redness with an eruption of minute papules within from 12 to 72 hours.

*Conjunctival Test.*—Another test for tuberculosis is that advocated by Calmette and which is made by instilling into the conjunctival sac a drop of a 0.5 per cent. aqueous solution of the old tuberculin. If tuberculosis is present conjunctivitis (not merely transient redness of the conjunctiva) ensues in from 6 to 24 hours. This test, while fairly reliable, is not altogether free from danger, severe keratitis having been noted in a few cases. Even the slightest affection of the eyes should be regarded as a contraindication.

## General Miliary Tuberculosis

**Etiology.**—This condition, which is characterized by an eruption of numerous tubercles in various organs, pronounced toxic phenomena, and a rapidly fatal course, is caused by the free communication of a tuberculous focus with the general circulation and the discharge of large numbers of bacilli into the blood. The portal of entry is often a branch of the pulmonary vein which has become eroded by a contiguous caseous lymph-node. In other cases, probably the majority, the bacilli appear to be liberated in the blood stream from a tuberculous nodule that has been formed in the thoracic duct or in a blood-vessel, especially one of the pulmonary veins or the aorta. The thoracic duct may be involved by drainage from infected lymph-nodes through the lymphatics, or by direct contact with a cheesy mass. Vascular tuberculosis develops from the implantation upon the intima of the vessel of bacilli carried there by the blood stream, or less frequently from the direct extension of a lesion in close association with the vessel. The bacilli do not multiply in the blood, but in the tissues to which they are borne.

General miliary tuberculosis is seen most frequently in persons who have chronic tuberculosis of the lungs, lymph-nodes, bones or joints, and is more common in children and young adults than in older subjects. Not rarely it follows some other acute infection, such as measles, whooping cough or typhoid fever. Certain chronic diseases such as cirrhosis of the liver, diabets, etc., by lessening resistance also favor its occurrence. In some instances the widespread dissemination of the bacilli is brought about by trauma or by surgical operation on localized tuberculous lesions, especially of the bones or joints.

**Morbid Anatomy.**—The tubercles are widely distributed, although they often predominate in one organ or tissue. The lungs, the liver, and the spleen usually present the greatest number, but in the majority of cases the serous membranes, the kidneys, the choroid coat of the eye, and the bone-marrow are also more or less affected. On the other hand, the tissues of the stomach, pancreas, myocardium, uterus, voluntary muscles and skin are not often involved. As a rule, the tubercles are very numerous, small, and of about the same age, indicating that there has been one overwhelming invasion of the blood by bacilli, with the production of an acute infection of a few weeks' duration. In some instances, however, the tubercles occur sparingly, are of different ages and sizes, and are associated with a few caseous masses scattered here and there through the viscera. In such cases the infection has usually been subacute and probably brought about by several successive immigrations of bacilli in relatively small numbers.

**Symptoms.**—The symptoms of general miliary tuberculosis depend in part upon the general infection and in part upon the local lesions. Either group may predominate. The general symptoms resemble those of typhoid fever and the local symptoms usually point especially either to the lungs (pulmonary form) or to the brain (meningeal form), but they may be referable to some other organ or point equivocally to several organs.

*General Symptoms.*—The disease may set in quite suddenly with chills, headache and fever, but usually there is a history of lassitude, weakness and anorexia extending over a period of ten days or two weeks. Evidence of chronic or latent tuberculosis frequently exists somewhere in the body. The temperature is usually high and may reach 104° or 105° F. It is exceedingly irregular and the diurnal exacerbations and remissions are generally more marked than those of typhoid fever. Exceptionally cases are observed in which there is little or no fever. The pulse is accelerated, from 110 to 130, weak and occasionally dicrotic. The respirations are hurried, often out of proportion to the fever, but the physical signs may not indicate more than a catarrhal condition of the large bronchi. Cough, unproductive or accompanied by mucopurulent expectoration, may also be present. The tongue is furred and tympanites and diarrhea are sometimes noted as in typhoid fever, but less frequently. The spleen is usually enlarged. The urine is scanty high-colored and often slightly albuminous. The diazo reaction is present in many cases. Absence of leucocytosis is the rule unless there is extensive involvement of the meninges or a complicating pyogenic infection. Tubercle bacilli are occasionally found in the blood. The skin is generally pale, but with the pallor there is often a definite cyanotic hue. Profuse sweating, especially at night, is observed in many cases. Herpes, which is rare in typhoid, is common in miliary tuberculosis. Tileston[1] has called attention also to the not infrequent occurrence of minute papules, capped with vesicles, and in which tubercle bacilli may sometimes be demonstrated. Occasionally a roseolar rash conforming closely to that of typhoid fever appears and very

[1] Archives of Internal Medicine, July 15, 1909.

rarely miliary tubercles develop in the skin. Certain nervous symptoms, especially headache, dizziness and somnolence, are usually observed early in the disease even when there is no infection of the meninges, and later delirium, stupor, subsultus, etc. may also supervene. These features, together with increasing weakness, emaciation, a dry tongue, and a distended abdomen make the resemblance to typhoid fever very close. Eventually, however, the nature of the case is usually made clear by the appearance of certain phenomena which are more or less characteristic of tuberculosis and which are due to the presence of tubercles in the lungs or meninges. Thus, marked dyspnea with signs of insular consolidation of the lungs may arise or there may be definite indications of meningitis, such as rigidity of the neck, Kernig's sign, paresis of the ocular muscles, an eruption of tubercles on the choroid, etc. Reckoning from the onset of severe symptoms, the duration is usually from 2 to 6 weeks, but occasionally the course is prolonged to several months, the symptoms until a late period consisting chiefly of slight fever, headache, malaise, and gradually increasing weakness, anemia and emaciation.

*Pulmonary Symptoms.*—In some cases of general miliary tuberculosis the pulmonary symptoms overshadow those of the general infection. In such cases the onset is often abrupt and suggestive of simple bronchopneumonia. The temperature is moderately high, the pulse is rapid (120–140) and cough and dyspnea are pronounced. In the early stages the expectoration is scanty and consists chiefly of mucus, sometimes bloodstreaked or rusty as in croupous pneumonia. Later, there may be mucopurulent sputum. Cyanosis, out of proportion to any objective findings, is often observed and is a significant feature. Pleuritic pains, due to the presence tubercules in the pleura, are not uncommon. In the absence of antecedent pulmonary tuberculosis the physical signs are usually those of a severe capillary bronchitis (bronchopneumonia). The percussion note is frequently hyper-resonant from over distention of the lungs, but occasionally there are small areas of dulness, corresponding to patches of consolidation. The breath sounds are somewhat harsh and accompanied by numerous fine moist râles which are especially marked after coughing. Friction-sounds may sometimes be detected. Tubercle bacilli are rarely found in the sputum unless the acute process has supervened upon the softening of a chronic tuberculous focus. Death may occur in the course of a fortnight or the symptoms may abate somewhat and the disease be prolonged to a month or six weeks.

*Cerebral Symptoms.*—When meningeal infection is present the cerebral manifestations are often so pronounced that the disease is believed to be one of meningitis rather than of general tuberculosis. The predominant symptoms are fever, headache, vomiting (projectile), rigidity of the neck, convulsions or local muscular twitchings, and disturbances in the innervation of the ocular muscles (anisocoria strabismus, ptosis, etc.). In the early stage the respirations are sometimes exceedingly rapid and toward its close Cheyne-Stokes breathing is present in many cases. The tache cérébrale is well marked, but is without diagnostic significance. Optic neuritis is sometimes present and not rarely tubercles may be found in the choroid. Kernig's sign and Brudzinski's sign may usullay be elicited. The spinal fluid is under increased pressure and is clear at first, but often yields a filmy coagulum on standing. It usually presents a preponderance of lymphocytes except in the later stages when polymorphonuclear cells may be in excess. Tubercle bacilli may be found in the fluid in a large proportion of cases. Death ensues usually in from ten days to three weeks.

**Diagnosis.**—In many cases the diagnosis is readily made, but in other

cases it is difficult or even impossible. It is based upon the occurrence of persistent irregular fever and gradually increasing general symptoms without obvious local cause and without the characteristic features of typhoid fever or septic infection. The presence of an antecedent tuberculous affection in some part of the body, a previous history suggestive of tuberculosis, or the occurrence of the symptoms soon after an attack of measles or whooping cough is important evidence. The appearance of marked dyspnea and cyanosis without adequate explanatory physical signs or of meningitic symptoms in the course of an obscure fever is extremely suggestive, and the detection of choroidal tubercles or of tubercle bacilli in the spinal fluid or blood is conclusive. The diagnosis from typhoid fever is considered on page 106, from ulcerative endocarditis on p. 674 and from pneumonia on p. 79.

*Treatment.*—The treatment is purely palliative. In the typhoid form the general management should be that of typhoid fever. When the pulmonary symptoms predominate local applications to the chest and cough sedatives are indicated. In the meningeal type the treatment coincides with that of tuberculous meningitis.

## Tuberculosis of the Respiratory System

### Tuberculosis of the Nose, Larynx and Trachea

**Tuberculosis of the nose** is rare and usually secondary to tuberculosis of the lungs. As a rule, it takes the form of an ulcer that spreads slowly or rapidly, sometimes involving the cartilages and bones. The septum is the favorite site of the lesions. Occasionally a polypoid growth composed of tuberculous granulation tissue (tuberculoma) appears instead of an ulcer.

**Tuberculosis of the larynx** is usually observed as a complication of advanced pulmonary tuberculosis, but occasionally it develops early in the course of the lung disease and in very rare instances it appears to be primary. The larynx is involved sooner or later in more than one-fourth of all cases of clearly defined pulmonary tuberculosis. The medium of infection is probably, as a rule, the sputum, but it may be the blood or the lymph, or, in the rare primary form, the inspired air. According to the stage of the process, the changes in the larynx may consist of hyperemia or anemia of the mucous membrane, infiltration of the subepithelial tissues, or ulceration. The structures most frequently attacked are the arytenoids, the interarytenoid space, and the epiglottis.

*Symptoms.*—The usual subjective symptoms are hoarseness or aphonia, cough, and pain on swallowing. The dysphagia is rarely marked, however, unless the epiglottis or the aryteno-epiglottic folds are affected. In the early stages the mucous membrane is more often pale than florid, and in many cases the pharynx and soft palate share in the anemia. Infiltration is most frequently shown in the arytenoids, which may be transformed into rounded or clubbed-shaped swellings. Fungous-like excrescences are sometimes observed on the interarytenoid folds or commissure. When the epiglottis is uniformly infiltrated the swelling is characteristically turban-shaped. The ulcers usually are multiple and irregular in outline, giving to the parts a worm-eaten appearance. As a rule, they are shallow and pale and show little tendency toward cicatrization. The mobility of the vocal cords is frequently impaired, either by the infiltration or by paresis of the recurrent laryngeal nerve.

The *diagnosis* should be based not only upon the appearance and course of the laryngeal lesions, but also upon the history, the bacteriologic findings,

and the results of the physical examinations of the lungs. Syphilitic and malignant ulceration must be excluded. In syphilis the destruction of tissue is much more rapid and the ulcer, which is usually solitary, is likely to be deep, sharply defined, and bordered with a zone of inflammatory induration. Occasionally a syphilitic ulcer becomes tuberculous. In carcinoma the lesion is primarily unilateral and appears as an ulcerating outgrowth rather than as a shallow excavation, and the surrounding tissue is markedly inflammatory and edematous.

The *prognosis* should always be guarded, although much can be done when the disease is still in an early stage to effect a cure or to retard its progress. Important factors to be considered are the condition of the lungs, the state of the general health, and the character and location of the laryngeal lesions. Generally speaking, the outlook is less favorable when the epiglottis and aryepiglottic folds are involved than when the lesions are within the larynx.

*Treatment.*—The general treatment should be that of pulmonary tuberculosis. Vocal rest is essential. Inhalations of creosote, compound tincture of benzoin and eucalyptol are of service in relieving cough. In the milder cases of infiltration or ulceration applications or instillations of menthol (1 per cent. in olive oil) or of argyrol (10 to 30 per cent. solution) will be found useful. When the infiltration is marked the affected parts may be cocainized and then thoroughly rubbed with lactic acid in glycerine (5 per cent., gradually increased as tolerance is established to 50 per cent. or more) or, preferably, punctured in one or more places with the white-hot galvanocautery needle. Refractory ulcers may also be cauterized with the galvanocautery or with lactic acid. When the disease is far advanced only sedative applications to relieve pain and dysphagia are justifiable. Insufflations of orthoform, anesthesin or iodoform are especially useful. Rebuck of Pennsylvania State Sanatorium at Mont Alto speaks favorably of free applications of the following emulsion:

| | |
|---|---|
| ℞ Mentholis | gr. xl (2.5 gm.) |
| Olei amygdalæ expressi | f℥vi (22.5 mils) |
| Ovi vitelli | f℥iv (15.0 mils) |
| Orthoform | ℥ii (8.0 gm.) |
| Aquæ destillatæ | qs. ad. f℥ii (60.0 mils). M. |

If the dysphagia is very severe it may be advisable to apply cocain before eating, using a 2–5 per cent. solution as a spray or a 5–10 per cent. solution as a direct application. Wolfenden's method of feeding may also afford relief. The patient lies prone with his head hanging over the edge of the bed and while in this position takes liquid food through a tube from a bowl that is placed on the floor or a stool.

**Tuberculosis of the trachea** is rare and almost always secondary to lesions in the lungs or larynx, the sputum being, as a rule, the medium of infection. The disease usually begins with the formation of small tubercles, which eventually break down, leaving shallow ulcers resembling those of tuberculous laryngitis.

## TUBERCULOSIS OF THE LUNGS

**Forms.**—Tuberculosis of the lungs may be an acute or a chronic process. The latter is by far the more common. Of the acute varieties, two groups may be recognized: (1) Acute miliary tuberculosis and (2) acute pneumonic tuberculosis. Chronic pulmonary tuberculosis may also manifest itself in one of two forms: (1) Chronic ulcerative tuberculosis and (2) chronic fibroid

tuberculosis. It is to be remembered, however, that cases intermediate between these forms often occur.

### Acute Pulmonary Tuberculosis

(Phthisis Florida; Galloping Consumption)

**Morbid Anatomy.**—The widespread occurrence of miliary tubercles in the lungs is often a part of a general tuberculosis, although the disease may be most extensive in the lungs. The tubercles, which vary considerably in number in different cases, are found both in the connective tissue about the vessels and bronchi and in the parenchyma of the organ. The tissue between them may be unchanged or slightly congested and edematous, but commonly the alveoli surrounding the larger nodules are filled with a catarrhal or fibrinous exudate.

Acute pneumonic tuberculosis usually depends upon the inhalation of bacilli or upon the aspiration into the bronchi of infective material from a preexisting tuberculous focus in the lung itself or in the adjacent lymph-nodes. The smaller bronchi and the associated groups of air-cells are affected, producing nodules of consolidation ranging in size usually from a pea to a walnut (*lobular tuberculous pneumonia*). The more recent nodules are grayish-red and the older ones are grayish-yellow, with, perhaps, central softening. The adjacent tissue is frequently reddish, sunken and collapsed as in ordinary bronchopneumonia. Definite tubercles may or may not be present. In the beginning the exudate is found to consist of epithelial cells, leucocytes, red corpuscles, and perhaps fibrin. Later, after the occurrence of necrosis and caseation the whole consolidated area is transformed into structureless detritus. The highly resistant elastic fibers of the lung remain for a time, but ultimately all the tissue elements, including the walls of the bronchioles, undergo disintegration and caseation. Many alveoli contiguous to the consolidated areas are filled with fluid exudation in which float fatty epithelial cells. Mixed infection is common and as alresult areas of simple bronchopneumonia due to streptococci, pneumococci, etc. are often present. Occasionally when many tubercle bacilli enter the bronchi at one time a whole lobe or even a whole lung may become uniformly solidified as in ordinary lobar pneumonia (*lobar tuberculous pneumonia*). The tuberculous nature of the process is indicated however by the peculiar translucent and gelatinous appearance of the tissue that is not so intensely affected, by the small amount of fibrin and the comparatively large number of epithelial cells in the exudate, and, above all, by the marked tendency of the exudate to undergo caseation. If the course is not too short extensive disintegration may occur with the formation of large irregular cavities. With the acute lesions, evidences of older tuberculosis may often be found.

**Symptoms.**—The symptoms of *acute miliary tuberculosis of the lungs* are much the same as those of general tuberculosis with predominant pulmonary symptoms and are considered on p. 25. *Lobar tubercucous pneumonia* frequently sets in with the clinical picture of ordinary lobar pneumonia and in many cases it is only the subsequent course of the disease that leads to a correct diagnosis. Significant features are the absence of the crisis, the persistence of the physical signs with evidences of softening and excavation, the development of a remittent fever with sweating and rapid emaciation, and ultimately the occurrence of tubercle bacilli and elastic tissue in the sputum.

*Acute bronchopneumonic tuberculosis* occurs in children as well as in adults. In children it is observed most frequently after one of the infectious diseases,

especially measles or whooping cough. In adults it may occur in one who has been apparently well or in one who for some time has manifested more or less evidence of focal tuberculosis. The symptoms and physical signs are essentially those of simple bronchopneumonia and not rarely ten days or

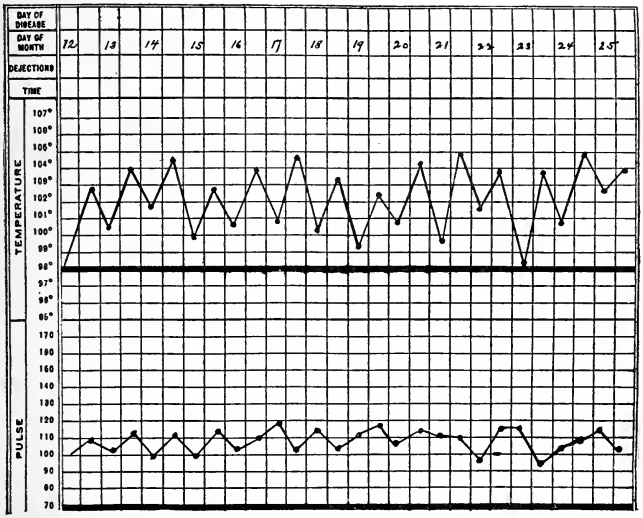


FIG. 1.—The temperature curve in acute pulmonary tuberculosis.

two weeks elapse before any suspicion of the real nature of the case is entertained. Evidence of previous tuberculosis in the lung or elsewhere in the body or a history of antecedent ill health and a tendency of the lesions to localize at the apices are important indications; so, too, are the failure of resolution to occur at the usual time, the replacement of the signs of consolidation by those of softening and excavation, the appearance of hectic fever with profuse sweats and recurrent chills, and the rapid occurrence of emaciation. The presence of tubercle bacilli and of elastic fibres in the sputum is, of course, irrefutable evidence, but it may not be obtainable until a late period.

The acute pneumonic forms of tuberculosis usually end fatally in from three to eight weeks. Occasionally, however, the severe symptoms abate to some extent and the disease becomes subacute or chronic.

### CHRONIC ULCERATIVE TUBERCULOSIS OF THE LUNGS

**Morbid Anatomy.**—Chronic ulcerative tuberculosis is by far the most common form of pulmonary tuberculosis. The disease almost always begins near the apex of the lung and then gradually spreads downward. In some instances, however, especially in children, the first lesion is at the base or in

the central portion of the lung. The special predisposition of the apex has been attributed to various factors such as deficient aëration, poor blood supply, inactive lymph current, immobility caused by a rigid first rib, etc. According to the stage of the disease the apical lesion may consist chiefly of a collection of gray or yellow tubercles, of a uniform cheesy mass, caused by the caseation and confluence of many tubercles, or of a cavity, brought about by the softening of a caseous mass and the discharge of its contents through a bronchus. Secondary infection by pyogenic organisms is largely responsible for the destructive changes. If healing has occurred the only finding at autopsy may be a small encapsulated caseous or calcareocaseous nodule or a small pigmented scar. When the conditions are not favorable to healing the disease gradually spreads from the original focus until it involves a large part of the pulmonary tissue. In persons dying of chronic pulmonary tuberculosis both lungs are usually affected, although not equally. The appearances observed after death vary in different cases according to the age of the lesions, the mode of dissemination and the degree of resistance offered by the tissues. In advanced cases one may find large and small cavities, large irregular areas of caseation, scattered patches of caseous pneumonia or of a reddish or reddish gray infiltration that has not yet reached the stage of caseation, many or few miliary tubercles, and a more or less extensive overgrowth of fibrous tissue, the last representing the attempt of nature to check the progress of the disease. The growth of tuberculous process may depend upon direct extension of the infection through the tissues, upon the transportation of bacilli by way of the lymphatics or bloodvessels, or upon the discharge of caseous material into contiguous bronchi and its insufflation into parts of the lung not yet diseased.

Tuberculous cavities vary from the size of a pea up to the size of a whole lobe. Enlargement is brought about by gradual liquefaction of a caseous mass, by true ulceration the result of mixed infection, or by fusion of adjacent excavations. The wall of the cavity may be covered with shreds of necrotic tissue or with a smooth "pyogenic membrane" and the contents may consist of thick caseous material or muco-pus. Nearly all cavities, except those of very small size, communicate with the bronchi. Bloodvessels, either patent or occluded, frequently traverse the cavity or ramify in its walls, and not rarely those that remain unoccluded become the seat of small aneurysms. It is from aneurysms of this character that the large hemorrhages of the later stages of tuberculosis usually take place, although profuse bleeding may also occur from the mere erosion of bloodvessels without aneurysmal dilatation.

Other lesions are usually found in the lungs in addition to those due to the tuberculosis itself. Thus, bronchitis is almost constantly present. Dilatation of the bronchi is also common, and some of the cavities may depend upon localized bronchiectasis rather than upon liquefaction of a caseous mass. Scattered areas of simple bronchopneumonia, the result of mixed infection, are sometimes observed and in the majority of cases parts of the lung that are not directly involved in tuberculous or pneumonic processes are the seat of compensatory emphysema. Pleuritic adhesions and thickenings are rarely absent. Serofibrinous pleurisy, empyema, and pneumothorax are also more or less frequently observed. Other organs besides the lungs are frequently involved in the tuberculous process. This is especially true of the larynx, intestines and kidneys. The lymph-nodes in relation to the lungs are almost invarlably affected. The abdominal viscera sometimes show amyloid change and the liver in many cases is fatty.

**Symptoms.** *Onset.*—Usually the onset is gradual, the first symptoms

in many cases being those of general ill health, with lassitude, ready fatigue, pallor, and loss of weight. In young women the pallor is sometimes very marked, and if amenorrhea is also present, which is often the case, the condition may readily be mistaken for chlorosis. Not rarely the patient seeks advice because of indigestion. General ill health, anemia or atonic dyspepsia occurring in a person with a slight but persistent evening rise of temperature and some acceleration of the pulse or with slightly abnormal physical signs at one apex is highly significant. More frequently the patient dates his illness from an attack or a series of attacks of bronchial catarrh which he has been unable to overcome. In some instances the early symptoms are ascribed to influenza rather than to a common cold and occasionally gradually developing hoarseness is the first suggestive feature. In other cases hemoptysis or an attack of pleurisy, dry or serous, is the first indication. Hemoptysis, without obvious cause, even if it occurs in the midst of apparent health, is almost certainly due to tuberculosis and so-called idiopathic pleurisy should always be viewed with strong suspicion.

Once the disease is definitely established, the symptoms are both *local* and *general*.

*Cough* is usually a conspicuous symptom, but its severity and character vary much in different cases. At first it may be nothing more than a clearing of the throat or it may be dry and hacking. As a rule, it is worse at night and on rising in the morning. Severe paroxysms after meals frequently lead to vomiting. In some instances cough does not appear until every other indication of tuberculosis is present and well marked, and occasionally it is absent until a few weeks before death. In many cases, even of advanced tuberculosis, the cough is to a great extent susceptible to voluntary control. The quantity and character of the *sputum* are also subject to much variation. At first the sputum is often scanty and composed chiefly of glairy mucus, but as the disease progresses it usually becomes abundant and mucopurulent. It comes from inflamed bronchi and in the later stages also from the walls of cavities. When the disease is well advanced it often takes the form of dense greenish-gray coin-like masses, which sink in water (nummular sputum) and not rarely it contains opaque cheesy particles visible to the naked eye. Tubercle bacilli appear in the expectoration sooner or later in almost all cases and their presence is conclusive evidence of tuberculosis, but it must be borne in mind that the bacilli are rarely found before some breaking down has occurred in the tuberculous deposit and consequently the disease may exist for weeks or months before the sputum examination is positive. Later, other organisms, such as streptococci, staphylococci, pneumococci, and influenza bacilli, are also found. In addition to bacteria, fibers of elastic tissue are often recognized in tuberculous sputum that has been boiled with caustic soda and centrifugalized. This finding has much significance, although it also occurs with pulmonary abscess and gangrene of the lung. The sputum of tuberculosis usually contains more albumin than that of other pulmonary diseases, but this feature is of no practical value in diagnosis.

*Hemoptysis* occurs at some period or other in about 50 per cent. of all cases. It is uncommon, however, in young children. Sometimes it is the first indication of the disease but more frequently it comes on at a later period. The bleeding may occur without any apparent exciting cause, or it may follow physical or mental excitement, and not rarely it seems to be due to some intercurrent infection. In institutions cases often occur in groups. Recurrences of hemorrhage over periods of days or weeks are common. The bleeding may be only sufficient to streak the sputum or it may be very

profuse, the patient bringing up a pint or more of blood in a short time. It may be so profuse, indeed, that death suddenly occurs from suffocation or collapse. This, however, is rare, and in some cases, bleeding, if moderate, actually proves beneficial, at least temporarily. It is likely that slight hemorrhages are due to pulmonary congestion and the larger ones to erosion of bloodvessels within cavities. Localized pain and tenderness are not uncommon accompaniments of hemoptysis and in some instances the bleeding is followed by pneumonia. General miliary tuberculosis is a rare sequel.

*Pains in the chest* are common in pulmonary tuberculosis and may be pleuritic or muscular, the latter being often the result of cough. The respiratory rate is usually increased and *dyspnea* is frequently present, although many patients make little complaint of their breathing despite extensive changes in the lungs. Pronounced shortness of breath may be due to peculiar sensitiveness of the respiratory center to the toxins, to some pulmonary complication, such as emphysema, pleurisy, pneumothorax or secondary bronchopneumonia, or to profound anemia.

*Fever* is present, as a rule, in all active cases, and in persons whose general health is somewhat impaired or who have cough, persistent elevation of temperature, no matter how slight, should always arouse suspicion if other causes of pyrexia can be excluded. In incipient cases, when the diagnosis is in doubt, the temperature should be taken, if possible, every two or three hours, for several days. Occasionally in the early stages, the temperature is elevated only after exercise or in women at the time of menstruation. The fever is usually of a remittent or intermittent type, and when the disease is well established the temperature in the afternoon or evening may be 102° or 103° F. and nearly normal or even considerably below normal in the morning (hectic fever). During the exacerbations patients frequently present flushed cheeks and complain of chilliness, lassitude or other unpleasant sensations. High temperatures are generally attributable to mixed infection. In chronic stationary tuberculosis there is often no fever for long periods and occasionally even with rapidly advancing caseation the temperature is normal or nearly normal.

*Acceleration of the pulse* occurs at an early period and sometimes may be noted in advance of any definite pulmonary symptoms or signs. In the early stages of the disease the pulse rate is often 85 or 90 and in the later stages of the disease it is usually 100 or more. Frequently the pulse is more disturbed than the temperature. The pulse tension is generally subnormal. With increasing weakness of the circulation it is not uncommon for some degree of edema to supervene. *Night sweats* occur at one time or another in the majority of cases. The tendency to sweating is mainly due to secondary infection, and hence it is especially marked while softening and excavation are under way. Complete rest in bed in a well ventilated room and an appropriate diet usually control it. *Chills* sometimes occur when the temperature is high. *Digestive disturbances*, such as a coated tongue, anorexia, eructations and vomiting, are an important feature in many cases and are more frequently the result of faulty gastric secretion or motility than of organic disease. Tuberculous ulceration of stomach is rare. Intestinal tuberculosis is a frequent complication, but it does not always cause definite symptoms; on the other hand, *diarrhea* and *abdominal pain*, which are sometimes conspicuous phenomena, are due in a considerable proportion of cases to functional disturbances of the bowel or to catarrhal enteritis. *Amenorrhea* occurs in more than one-fourth of the cases and is usually due to general weakness and anemia. It is beneficial rather than detrimental.

*Emaciation* is an important symptom and in advanced cases the patient's

weight may be reduced by a quarter or even a third. The loss of weight is chiefly due to the toxemia, although the fever, digestive disturbances, and sweating may be contributing factors. Exceptionally the general condition remains good for a long time, even when the physical signs indicate extensive changes in the lungs. Coincident with the emaciation, but not necessarily proportionate to it, there is a *failure of strength and energy*. Ultimately, in unfavorable cases, the weakness may be so extreme that the patient can scarcely turn in bed. Contrary to general belief, the *basal metabolic rate* in tuberculosis is not materially increased unless the temperature is high and the cough severe. Indeed, in afebrile cases the rate is often slightly lower than normal.

Tuberculous patients usually have a clear intellect until the end, and many are remarkably hopeful as to a favorable outcome, even when the disease is far advanced. Occasionally, however, evidences of disturbed mentality are observed toward the close in consequence of deficient nutrition and anemia.

Virtually all cases of pulmonary tuberculosis show some degree of *anemia*, the percentage of hemoglobin being more reduced, as a rule, than the number of erythrocytes. In cases not far advanced the percentage of lymphocytes is increased, but the whole number of leucocytes is about normal. In advanced cases there is usually a slight or moderate leucocytosis with an increase of the polymorphonuclear cells at the expense of the lymphocytes. Arneth,[1] claims that in cases with low resisting power there is a preponderance of neutrophiles with one or two nuclei, while in cases with good resisting power the percentage of neutrophiles with three, four and five nuclei is increased. This claim has been supported by a number of observers (Arloing and Gentry, Edson, Klebs, Bushnell and Treuholtz, Minor and Ringer). Although tubercle bacilli undoubtedly gain access to the blood from time to time, the number present at any given moment is so small that it is rarely possible to demonstrate them even by animal inoculation.

A moderate degree of *albuminuria*, with or without the presence of hyaline and granular casts, is frequently observed, especially in the later stages of the disease.

**Physical Signs.**—There are no physical signs peculiar to pulmonary tuberculosis, but in their localization, combinations, evolution and association with symptoms certain signs furnish almost conclusive evidence of the disease. The changes in the lungs are almost always more extensive, however, than the physical signs indicate, and occasionally the lesions evade detection by physical methods when the symptoms and bacteriologic findings point unequivocally to tuberculosis. In examining the chest it is advisable to have the patient stripped to the waist, seated or standing, and in a good light. It is also important to compare corresponding points on the two sides and to bear in mind that in the majority of healthy persons the vocal fremitus and vocal resonance are more marked, the percussion note is higher in pitch and slightly less resonant, and the expiratory breath sounds are somewhat more distinct and prolonged over the upper part of the right lung than over the corresponding area on the opposite side. The differences in the physical signs over one apex as compared with the other are apparently due, as pointed out by Fetterolf and Norris,[2] to the immediate contact of the trachea with right pulmonary apex and to the encroachment of the large vessels upon this apex.

[1] Die Neutrophilen weissen Blut Korperchen bei infections Krankheiten, Jena, 1904.
[2] Amer. Jour. Med. Sci., May, 1912.

*Inspection.*—The chest may be well-formed in every respect, but in many cases it is abnormally long, flat and narrow, with deep supra- and infra-clavicular foissæ, wide intercostal spaces, a very acute epigastric angle and prominent (winged) scapulæ. This so-called phthisinoid chest is probably the result of tuberculosis in early life and not, as was formerly believed, a congenital condition predisposing to the disease.

Diminished expansion or retardation of the respiratory movements over one apex is an early sign and is often best observed by standing behind the patient and looking down upon the front of his chest. At a later stage there is frequently more or less asymmetry of the upper part of the thorax, particularly in the direction of flattening above or below one of the clavicles. This depression may depend upon local atrophy of the superficial tissues, pleural adhesions, fibroid changes in the lung or the presence of cavities. Not rarely the cardiac impulse is displaced to one side, usually the left.

Changes in the fingers are frequently observed, especially in long-standing cases; thus the nails may be curved foreward, the fingers may be long, slim and tapering or the terminal phalanges may be markedly thickened (clubbed fingers). This last change, which is not peculiar to tuberculosis, is probably due to the selective action of certain toxic substances and to peripheral venous stasis. In many instances the nature of the illness is at once suggested by the general appearance of the patient particularly by the wasted frame, the long and slender neck, the delicate skin, the bright eye, and the flushed cheek.

*Palpation.*—Any difference in expansion between the two sides may often be felt as well as seen. The vocal fremitus is not of much aid in early cases. Ordinarily it is increased over areas of consolidation and over large superficial cavities. It may be decreased, however, if there is pleuritic exudation, marked pleural thickening, or pneumothorax, or if the bronchi of the affected part are filled with secretion.

*Percussion* yields valuable information. Even in the very early stages there is frequently diminished resonance and as the infiltration progresses the dulness becomes more pronounced and extensive. In incipient cases special attention should be paid to the supra- and infra-clavicular areas, the outer half of the clavicles, the supraclavicular fossæ and the upper axillary regions. In comparing one side of the chest with the other, corresponding areas should be examined and all the muscles should be completely relaxed. Occasionally the infiltration is masked for a time by compensatory emphysema. With cavity formation the percussion note frequently changes. If the cavity is not too small, is near the surface, and contains chiefly air, it usually yields a muffled tympanitic note or a cracked-pot sound (bruit de pôt fêlé). The latter is obtained especially over cavities that communicate freely with a bronchus and may be elicited by percussing heavily over the suspected area while the ear is held close to the patient's open mouth. It may sometimes be produced also over the lungs of a crying child, and over relaxed lung adjacent to a pleuritic effusion or a pneumonic consolidation. The pitch of the percussion note over a cavity may vary according as the patient is in an upright or recumbent position (Gerhardt's phenomenon); it may be raised during inspiration and lowered during expiration (Friedreich's phenomenon); and it may be both raised in pitch and intensified when the patient opens his mouth (Wintrich's phenomenon), but these three points are of little practical importance.

Tenderness of the superficial tissues is frequently observed during percussion. It usually depends upon acute or chronic pleurisy, but it may be due merely to irritation of the nerve-endings in the thoracic muscles. Sharp

immediate percussion, especially over the pectoral muscle, often produces at the point which is struck a small quivering nodule or a linear sulcus running in the direction of the muscular fibres. This phenomenon, which is known as myoidema (Lawson Tait), is really physiologic, although it is likely to be more pronounced in tuberculosis and other wasting diseases than in health.

*Auscultation* yields results of great importance, even in very early cases. All portions of the lungs should be examined, but the first changes are usually to be found at one apex. There may be harsh breath sounds with prolongation of the expiration (bronchovesicular breathing) or there may be merely slight diminution in the intensity of the respiratory murmur. Respiration of the interrupted or "cogwheel" type is frequently heard and is significant if limited to one apex. Generalized cogwheel breathing may be the result of nervousness, fatigue or thoracic pain. As the infiltration extends and increases in density the respiration becomes distinctly bronchial, the expiratory sound being as long as or longer than the inspiratory, accentuated, and often of a blowing quality, and both sounds being somewhat harsh, of higher pitch than the vesicular, and separated from each other by an appreciable interval. Over open cavities of sufficient size there is usually cavernous or amphoric breathing, that is bronchial breathing with a hollow or metallic quality.

The occurrence of fine crackling or clicking râles over a limited portion of the lung, especially an apex, is a very early and important sign of pulmonary tuberculosis. These râles, which are the result of a localized bronchiolitis, are chiefly inspiratory, and in many instances cannot be heard unless the patient is made to cough. As the disease advances and secretion accumulates in the larger bronchi coarse moist râles or sundry types of musical râles may be heard, not only over the consolidated area, but over various portions of the chest. Large cavities may afford coarse bubbling or gurgling râles and exceptionally metallic tinkling. Pleural friction sounds may be audible at any period of the disease.

The vocal resonance, like the vocal fremitus, is usually increased over solidified areas and cavities. In some cases the voice sounds are not only much exaggerated, but appear to emanate from a point immediately beneath the ear or stethoscope (bronchophony), and in other cases even the articulate speech (both words and syllables) is distinctly transmitted through the chest-wall, especially when the patient whispers (pectoriloquy). Whispering pectoriloquy is very suggestive of a cavity, although it may sometimes be heard over solidified lung. Cardiorespiratory murmurs, probably dependent on variations in the intrathoracic pressure connected with the systolic contraction of the heart (Sahli), are not uncommon. Such murmurs may be heard along the left border of the heart, under the left clavicle, or below the angle of the left scapula, occur almost invariably during inspiration and in systole, and are much affected by breathing and posture.

*Roentgen examination* in skilful hands sometimes reveals changes in the lungs that cannot be detected by other means, although this method of study affords but little aid in distinguishing between active and quiescent tuberculosis. While a flat plate of the anterior surface of the chest and one of the posterior surface may be sufficient when only gross lesions are to be detected, stereoscopic plates are essential in early cases. Roentgenographic studies are especially useful in determining accurately the extent of the tuberculosis process and in detecting deep seated lesions when the physical signs are indefinite or equivocal. Among the early findings are haziness or fine mottling corresponding to the affected area, more or less restriction of the

movements of the diaphragm on the side of the lesions, and, especially in children, shadows cast by swollen bronchial lymph-nodes.

*The Combined Signs of Infiltration and of Excavation.*—The earliest physical signs are almost always apical and consist usually of diminution or lagging of the chest movement, slight dulness on percussion, the presence of fine crackling or clicking râles following cough, and weakness of the respiratory murmur, with or without interrupted inspiration, or harsh breath sounds with prolongation of the expiration. Extensive solidification is revealed, as a rule, by localized retraction of the chest wall and limitation of movement, pronounced dulness on percussion, exaggeration of the tactile fremitus and vocal resonance, and bronchovesicular or bronchial breathing. Râles of various kinds also are frequently audible. The most constant signs of an open cavity are localized retraction and deficiency of expansion, exaggerated tactile fremitus, a circumscribed tympanitic or cracked-pot note on percussion, cavernous or amphoric breathing, whispering pectoriloquy, and coarse bubbling râles.

**Complications.**—*Pleurisy* occurs at one time or another in nearly all cases. Any form of exudate may appear, but usually the inflammation is of a plastic nature and results in localized or general adhesions. *Pneumothorax*, total or partial, occurs in a small percentage of cases (3 to 6 per cent.), being much more frequent in males than in females. It is an exceedingly grave complication. *Pneumonia* in some form is frequent and may readily be overlooked. *Digestive disturbances*, due to perversions of the gastric secretion, motor insufficiency, gastrectasis, or chronic catarrh of the stomach are present in a large proportion of cases. *Diarrhea*, due to disturbances of digestion, to simple catarrhal enteritis, or to tuberculous ulceration of the intestines, is also common. *Chronic diffuse nephritis* is sometimes observed. *Venous thrombosis*, especially of the veins of the leg, and *peripheral neuritis* are occasional complications. With the progress of the disease tuberculosis is very likely to develop elsewhere in the body, especially in the intestines, larynx, kidneys, liver, spleen, peritoneum, and cerebral meninges. Anal fistulæ of tuberculous origin occur in from 2 to 6 per cent. of the cases. The liver frequently becomes fatty and in cases characterized by prolongd suppuration the abdominal viscera not rarely undergo amyloid degeneration.

**Diagnosis.**—The diagnosis of well-developed pulmonary tuberculosis presents little difficulty, but the recognition of the disease while it is still in the incipient stage is not always an easy matter. As inconspicuous and vague as the early symptoms may be, however, they are often strongly suggestive when considered together with a history of exposure to infection, the habits and mode of life, a deficiency in weight or thoracic development, and the results of careful physical examination of the lungs. The history or presence of scrofulous adenitis, of so-called idiopathic pleurisy, of anal fistula, or of suppurative otitis coming on painlessly is very significant in doubtful cases, and hemoptysis, in the absence of other causes, should be considered as due to pulmonary tuberculosis until proved not to be. Any one of the early physical signs mentioned on page 34 in association with failure of the general health, persistent cough, slight afternoon pyrexia or vague digestive disturbances points strongly to tuberculosis. It is noteworthy, however, that the progress of chronic pulmonary tuberculosis is almost invariably from the apex downward and that signs of infiltration completely localized at the base of a lung are with rare exceptions indicative of some process other than tuberculosis. In any case the presence of tubercle bacilli in the sputum is, of course, decisive, but it must not be forgotten that this evidence is not available until disintegration of the tuberculous area has

begun. The limitations of the tuberculin tests have already been considered (see p. 22). Attempts to discover a reaction based upon the presence of agglutinins and precipitins in the blood of tuberculous patients have so far led to no fruitful results.

Ordinary *chronic bronchitis* bears only a superficial resemblance to pulmonary tuberculosis. It is not accompanied by fever, pronounced weakness and emaciation, hemoptysis or signs of pulmonary solidification or excavation, nor does it respond to the bacteriologic tests for tuberculosis. Persistent bronchitis with the signs limited to one side or one part of the chest, however, should always arouse suspicion of tuberculosis. The differential diagnosis of *bronchiectasis* from pulmonary tuberculosis is frequently difficult, because bronchiectatic cavities yield the same physical signs as tuberculous cavities and, moreover, both conditions are often present in the same patient. Much importance is aitached to the clinical history and to the results of repeated bacteriologic examinations of the sputum. Bronchiectatic cavities, in contrast with those of tuberculosis, are usually basic and are not preceded or accompanied by signs of solidification. Another point in favor of bronchiectasis is the want of parallellsm between the general condition of the patient and the extent of the pulmonary changes as shown by the physical signs.

*Syphilis of the lungs*, although comparatively rare, often presents a clinical picture similar to that of pulmonary tuberculosis. Errors in diagnosis are not likely to occur, however, if the possibility of syphilis is constantly borne in mind. Any pronounced irregularity in the symptoms or physical signs or in the progress of the case should excite suspicion, but the most suggestive features of syphiils are the persistent absence of tubercle bacilli from the sputum, a positivc Wassermann test, and the presence elsewhere in the body of lesions that are probably syphilitic, such as periostitis, orchitis, iritis, ulceration of the throat, etc. The root and central part of the lung appear to be the favorite locations of syphilitic lesions, but too much stress should not be laid on this point, as the first signs of the disease are sometimes found at the apex.

Certain *subacute and chronic non-tuberculous pulmonary infections*, with Bacillus influenzæ, pneumococcus of Type IV, Staphylococcus albus, Streptococcus viridans, Bacillus mucosus capsulatus, or certain spirochetes (spirochæta bronchialis) in the sputum, may present many points of similarity to pulmonary tuberculosis. Series of cases of this type have been reported by Lord[1] Riesman,[2] Hamman and Wolman,[3] Miller,[4] Field,[5] Bloedorn and Houghton,[6] and others. The chief points against tuberculosis are the persistent absence of tubercle bacilli in the sputum and the presence of other organisms in large numbers; the localization of the lesions in the lower half of the lungs (very rarely at the apices); the good general health of the patient in comparison with the pronounced and extensive physical signs; and the lack of any tendency in the lesions to spread to other parts of the lungs.

*Aortic aneurysm* or *chronic cardiac disease*, especially mitral lesions with pulmonary edema and hydrothorax, and certain *sequelæ of pneumonia*, such as pulmonary abscess, delayed resolution and localized empyema, may be mistaken for tuberculosis of the lungs if the patient is under observation for only a short time. Among rarer conditions of the lungs that sometimes closely simulate pulmonary tuberculosis may be mentioned primary *malig-*

[1] Boston Med. and Surg. Jour., 1905, cliii, 537.
[2] Amer. Jour. Med. Sci., 1913, cxlvi, 313.
[3] Tr. Nat. Assn. Study and Prev. Tuberc., 1916, 171.
[4] Amer. Jour. Med. Sci., 1917, cliv, 805.
[5] Amer. Jour. Med. Sci., clix, 442.
[6] Jour. Amer. Med. Assoc., 1921, No. 23, 1559.

*nant disease*, *hydatid cysts*, *streptothrix infections*, and *distomatosis* (lung-fluke disease).

*Hyperthyroidism* and pulmonary tuberculosis have a number of symptoms in common, namely, tachycardia, loss of weight, sweating and possibly slight pyrexia, and in some instances it may be impossible to differentiate between the two conditions until the patient has been under observation for some time. The problem is rendered additionally difficult by the fact that symptoms of hyperthyroidism are sometimes present in incipient tuberculosis. In doubtful cases the determination of the basal metabolic rate is of very great help in diagnosis.

Ash[1] in 551 necropsy cases in which a clinical diagnosis of advanced pulmonary tuberculosis had been made found 61 (11 per cent.) that were non-tuberculous. The conditions present were cardiorenal disease, 27; pneumonic sequelæ, 11; neoplasm, 7; aneurysm, 6; syphilis, 4; septicemia, 4; actinomycosis, 1; pellagra, 1.

**Prognosis.**—The curability of pulmonary tuberculosis is attested by both clinical and pathological evidence. Indeed, it is well recognized that the disease frequently undergoes spontaneous arrest even in the absence of special treatment. Nevertheless, it is not always an easy matter to forecast the outcome in a given case, and in many instances it is unwise to express any definite opinion until the patient has been under observation for several weeks. As regards the disease itself much depends upon the extent of the pulmonary changes, the rate at which the process has advanced, the effect of the disease upon the nutrition, temperature and pulse, and the presence or absence of complications. As regards the individual himself the factors to be considered are age, environment, financial resources, intelligence, character, and temperament.

High temperature, undue acceleration of pulse, pronounced digestive disturbance and emaciation that fail to respond to rest and dietetic treatment are of evil omen. The number of tubercle bacilli in the sputum is not especially significant. Complications on the part of the kidneys, the heart, the digestive tract or the lungs themselves render the prognosis less favorable. Tuberculosis has little influence upon pregnancy, but pregnancy almost always exerts an unfavorable influence upon tuberculosis. A tuberculous ancestry is less important than was formerly believed, but a record of several deaths among brothers and sisters of the patient is suggestive of diminished family resistance to the disease. Generally speaking, young children and adults between 15 and 35 show less tendency to recover than persons at other ages. Underweight of the body has about the same significance as loss of weight. Intelligence sufficient to comprehend the nature of the disease and the manner in which its arrest may be brought about, willingness to cooperate with the physician, and strength of will to overcome many obstacles in the way of recovery are of great importance in the prognosis. Ample means to provide for personal wants and the wants of dependents, cheerful surroundings, and good sanitary conditions are conducive to recovery, but the better the surroundings under which the disease has been contracted the worse the prognosis. As a rule, improvement that has taken place under conditions of home life is more likely to be lasting than that which has taken place in a sanatorium. It must be borne in mind that relapse not rarely occurs after years of apparent health, and that enduring arrest of the disease is in large measure dependent upon continued careful living.

The average duration of life among patients with no advantages of proper environment, good food, and rest is about two years.

[1] Jour. Amer. Med. Assoc., Jan. 2, 1915.

### Chronic Fibroid Tuberculosis of the Lungs

Except in its acute forms, pulmonary tuberculosis is always associated with an overgrowth of fibrous tissue. Occasionally owing to the strong resistance of the patient or the low virulence of the infecting organism, the fibrosis is very pronounced and involves a large area of the lung. It is to this type of the disease that the term chronic fibroid tuberculosis is applied. The fibrosis usually starts at the apex of the lung, but it may begin in the pleura and extend inward along the interlobular septa. The affected lung is reduced in size and much tougher than normal. The bronchi are nearly always dilated. The pleura is adherent and thickened. The opposite lung is voluminous and the heart, which is usually displaced toward the affected side, frequently shows enlargement of the right ventricle. The tuberculous nature of the fibroid changes is, as a rule, revealed by the presence of caseous masses, apical cavities, or evidences of tuberculous infection in the opposite lung, but occasionally it can be demonstrated only by microscopic examination.

**Symptoms.**—Chronic fibroid tuberculosis lasts many years. When fully established, its chief symptoms are cough, mucopurulent sputum, occasional attacks of hemoptysis, and dyspnea on exertion. In many cases there is little or no fever. If large bronchiectatic cavities are present the cough may be paroxysmal and the expectoration abundant and fetid. Clubbing of the fingers is often marked. Despite the long duration of the disease—5 to 20 years—the general health may be but little impaired. In the last stages increasing dyspnea, swelling of the feet and other indications of cardiac dilatation often occur.

**Physical Signs.**—The chest wall on the affected side is retracted, sometimes to an extreme degree; expansion is deficient or absent; the spine is often curved laterally, and the heart is drawn toward the fibroid lung. The tactile fremitus may be exaggerated or entirely absent, according to the degree of pleural thickening. The percussion note is dull, except over cavities, where it may be tympanitic. The breath sounds may be bronchovesicular or bronchial, cavernous or amphoric, or feeble and distant, according to the degree of consolidation, the presence or absence of large cavities, and the amount of pleural thickening. Various râles are frequently heard. Cardiac murmurs are common, especially at the base of the heart. Over the unaffected lung the signs are those of compensatory emphysema.

Death may be due to intercurrent disease, failure of the right ventricle, profuse hemorrhage or miliary tuberculosis in the opposite lung.

Chronic fibroid tuberculosis may be indistinguishable from non-tuberculous fibrosis (cirrhosis) of the lung, although absence of tubercle bacilli from the sputum on repeated examinations and pronounced signs at the base with a relatively normal apex are in favor of the latter. The history is also helpful in the diagnosis, but it must be borne in mind that simple cirrhosis of the lung favors the development of tuberculosis by lowering the resistance of the tissue.

## TUBERCULOSIS OF THE PLEURA

Tuberculosis of the pleura is probably always secondary to tuberculosis in some other portion of the body, usually the lungs. Evidences of pleurisy are almost invariably found after death in pulmonary tuberculosis. The pleural cavity may contain a serofibrinous, hemorrhagic, or purulent exudate, but much more frequently the inflammatory process is fibrogenic and results in localized or general adhesions or in complete obliteration of the pleura,

the membranes being firmly united and the lung everywhere attached to the chest wall and diaphragm. In some instances tuberculosis of the pleura occurs without apparent involvement of the lung; indeed, it seems to be well established that the large majority of cases of so-called idiopathic pleurisy, that is of pleurisy developing without obvious cause, or without obvious cause other than exposure to cold, are actually tuberculous (see p. 612). In these cases it is likely that a minute tuberculous focus is really present in the lung, or that the bacilli are brought to the pleura by the lymphatics from infected bronchial or mediastinal lymph-nodes or are conveyed by the blood from some remote part. Microscopic examination of the effusion in this form of pleurisy may be negative, as the bacilli are usually present in comparatively small numbers. The tuberculous nature of the process may be shown, however, by inoculating animals with considerable quantities of the effusion (15 c.c.) and also by the preponderance of lymphocytes in the fluid after centrifuging and staining. Tuberculous pleurisy is sometimes due to the extension of a tuberculous process in the bones of the chest, in the pericardium or in the peritoneum. It also occurs as a part of general miliary tuberculosis.

Tuberculosis of the pleura may be acute or chronic. The latter may be a sequel of the acute form or it may develop insidiously. Anatomically, there may be (1) an eruption of tubercles without accompanying inflammatory lesions, (2) an eruption of tubercles with an abundant collection of clear serum in the cavity, (3) an exudate of fibrin, with or without an effusion of serum or pus, and with tubercles appearing beneath the fibrin or in the granulation tissue that is replacing it, or (4) if the resistance is high, partial or complete obliteration of the pleural sac, with transformation of the two layers of the pleura into thick fibrous plates that show little or no evidence of tuberculosis. The last form may be a part of a general serositis. In rare instances the pleural surfaces are studded with large nodular masses of translucent granulation-tissue, similar to that observed in the "pearl-disease" of cattle.

The *symptoms* of tuberculous pleurisy are essentially those of pleurisy arising from other causes. The *prognosis* depends largely upon the extent and degree of activity of the infection in other parts of the body, especially in the lungs. The tendency of so-called idiopathic pleurisy, despite its usual tuberculous origin, is toward recovery, although in a certain proportion of cases, probably not less than 25 per cent., manifestations of tuberculosis eventually appear in the lungs or other parts of the body.

## Tuberculosis of the Digestive Tract and Peritoneum

### Tuberculosis of the Mouth, Pharynyx, Tonsils, Esophagus and Stomach

Tuberculosis of the **mouth** is rare and usually involves the tongue. In 1916 J. R. Scott[1] collected 231 cases of lingual tuberculosis. Lingual tuberculosis may appear as a small circumscribed nodule (tuberculoma) or as a short fissure with two or more branches, although eventually it is likely to take the form of a shallow, sharply defined, indolent ulcer, with slightly beveled and undermined edges, and a yellowish-gray base. The free border of the tongue near the tip is the favorite seat of the lesion. The lymph-nodes below the jaw are not often affected and for a time there may be very little pain. Tubercle bacilli may sometimes be demonstrated in material from

[1] Amer. Jour. Med Sci., Sept. 1916.

lesion by microscopic examination or by animal inoculation. Syphilis may usually be excluded by the shallowness of the ulcer, the absence of other evidences of syphilis, and a lack of response to anti-luetic treatment. The exclusion of carcinoma is sometimes difficult. Slight pain, a lack of induration around the ulcer, and an absence of adenopathy are against carcinoma. The age of the patient may also be important.

Tuberculosis of the **pharynx** is rare and as a primary affection almost unknown. Tuberculosis of the tonsils is not uncommon. It may be primary, resulting from the direct lodgment of tubercle bacilli in the tonsil, but in the majority of cases it is secondary and has its origin in bacilli-laden sputum from the lungs or larynx.

How frequently the **tonsils** serve as the portal of entry into the body for tubercle bacilli is not definitely known. It has been demonstrated that these organisms may enter and pass through the tonsils and cause tuberculosis of the cervical lymph-nodes, while the tonsils themselves may escape injury, but as there is no direct communication between the cervical lymph-nodes and the pulmonary lymphatics it is unlikely that primary infection of the tonsils plays a very important part in the etiology of pulmonary tuberculosis. Tuberculosis of the tonsils is usually a microscopic finding. In some cases, however, the tonsil is enlarged and caseous foci are present. Occasionally ulceration is also observed. In 106 cases of tuberculosis of the cervical lymph-nodes A. P. Mitchell[1] found that the tonsils were definitely tuberculous in 38 per cent. In no instance was the appearance of the tonsil suggestive.

Tuberculosis of the **esophagus** is rare. It is usually due to erosion of the esophageal wall by a tuberculous lesion in an adjacent lymph-node or in the vertebræ, but it may result from infection of the esophagus by tuberculous sputum, or occur as a part of a generalized tuberculosis, the blood acting as the carrier of the infection. Occasionally tuberculosis is engrafted on a previous lesion, such as carcinoma or syphilis.

Tuberculosis of the **stomach** is uncommon and as an isolated primary condition exceedingly rare. In 2501 gastric operations at the Mayo Clinic tuberculosis of the stomach was found only once. The relative immunity of the organ probably depends upon its motility, the acidity of the gastric juice and the scarcity of lymphoid follicles in the walls of the stomach. The carrier of the infection is usually sputum from a diseased lung, but it may be the blood. The lesions may consist of ulcers, miliary or conglomerate tubercles, or tumor-like masses of scar tissue. The pyloric region is the favorite seat. Clinically, the condition is likely to be mistaken for simple round ulcer or for carcinoma. Of the 147 cases of tuberculous ulceration collected by Arloing[2] perforation occurred in 13.

## TUBERCULOSIS OF THE INTESTINE

Tuberculosis of the intestine may be primary or secondary. The *primary form* is rarely observed in adults, although it is not very uncommon in children. The source of primary intestinal infection is usually the milk of tuberculous cows, but it may be food that has been contaminated with the sputum of a tuberculous patient. Enterogenic infection does not necessarily lead to tuberculosis of the intestine. In many cases the bacilli apparently pass through the wall of the bowel without producing any demon-

[1] Jour. Path. and Bact. 1917, 21, 248.
[2] Arloing, "Les ulcerations tuberculeuses de l'estomac," Paris, 1903.

strable lesion at the point of entrance, and are then carried by way of the lymphatics to the mesenteric nodes, where they set up a focus of disease, or by way of the lacteals, thoracic duct and veins to the lungs, where they may be retained and cause characteristic lesions.

*Secondary tuberculosis of the intestine* is a common sequel of pulmonary tuberculosis, occurring in at least two-thirds of all cases of the disease that reach an advanced stage. It is usually due, no doubt, to the swallowing of tuberculous sputum, although it is possible that the bacilli may sometimes reach the intestine by the bloodstream, as occurs in cases of acute general miliary tuberculosis. While the colon rarely escapes, the lesions are, as a rule, most numerous in the small intestine above the ileocecal valve and in the cecum, probably because these parts are so rich in lymphoid tissue. Ulceration is the usual postmortem finding, but miliary or conglomerate tubercles or fibroid thickening may occur. The ulcers have a punched-out appearance with irregular, thickened, undermined edges, are not sharply limited to the Peyer's patches and solitary follicles, like those of typhoid fever, and, by following the course of the bloodvessels and lymphatics, tend to extend transversely to the long axis of the bowel, which occasionally is completely encircled. The serous membrane opposite the ulcers is often studded with miliary tubercles, and about these there are often fibrinous deposits or local adhesions. The mucous membrane around the ulcers may or may not be congested. Tuberculous peritonitis may develop in various forms. Perforation is rare (2 to 3 per cent. of the cases). When it occurs, it may result in diffuse peritonitis, local abscess, or a fistulous communication with another loop of intestine, some other viscus, or the surface of the body. A rectal or anal fistula not rarely results from the perforation of a tuberculous ulcer in the rectum. The proportion of cases of pulmonary tuberculosis presenting this complication varies, according to different observers, from 3 to 6 per cent.

An interesting but unusual, form of intestinal tuberculosis is that characterized by marked hyperplastic changes in the wall of the bowel without notable caseation or ulceration. It usually affects the cecum and results in the formation of a solid tumor-like mass and in a variable degree of intestinal stenosis.

The *symptoms of tuberculous ulceration of the intestine* are indefinite. Diarrhea, persistent or alternating with constipation, abdominal pains, and tenderness are often present. The stools sometimes contain blood, but rarely in large quantity. Emaciation is usually marked when the diarrhea is protracted. Tubercle bacilli are often found in the stools, but are not especially significant, as they usually come from swallowed sputum. It is noteworthy that all the symptoms presented may occur in tuberculous patients as a result of a simple catarrhal enteritis and, on the other hand, that numerous tuberculous ulcers may occur in the bowel without producing diarrhea or other clinical manifestations. Brown and Sampson[1] have found roentgenologic studies helpful in the diagnosis of colonic tuberculosis, the significant findings being hypermotility and spasm, or filling defects. The condition is usually progressive and terminates in death, although in some cases healing of the ulcers ensues. Stricture of the intestine is not a very rare sequel. It may be due to a contracting cicatrix or to a hyperplastic thickening of the bowel around an unhealed ulcer.

The *symptoms of the hyperplastic form of cecal tuberculosis* are those of gradually increasing stenosis of the bowel with the presence of a palpable tumor in the right ileo-cecal region. The diagnosis is sometimes possible from the evidences of pulmonary tuberculosis and the long duration of the

[1] Jour. Amer. Med. Assoc., July 12, 1919.

intestinal symptoms. The diseases with which the condition is most likely to be confused are chronic appendicitis and carcinoma of the cecum.

The *treatment* of intestinal tuberculosis is that of tuberculosis in general. For the diarrhea, rest in bed, careful regulation of the diet, and the administration of bismuth subnitrate or subgallate with tannigen or tannalbin are among the more useful measures. In hyperplastic cecal tuberculosis operation has sometimes yielded very good results.

## TUBERCULOSIS OF THE LIVER

Tuberculosis of the liver may be primary or secondary; the former is exceedingly rare. Infection may occur by way of the hepatic artery—the usual path in cases of acute general miliary tuberculosis; by way of the portal vein from tuberculous lesions in the intestine or spleen; and possibly, in very exceptional cases, by way of the lymphatics. The lesions may be in the form of miliary tubercles or large caseous masses (solitary tubercles). A tuberculous cirrhosis of the liver, showing tubercles in the newly-formed connective, has also been described. Miliary tubercles are found in the liver in at least 75 per cent. of all fatal cases of pulmonary tuberculosis, and, as a rule, appear to be the result of a terminal infection. Although known as solitary tubercles, the large caseous masses are frequently multiple. Such masses may soften and then break into the bile-ducts, setting up tuberculous cholangitis and leaving behind caseating cavities, or after softening they may still remain intact and thus appear as so-called tuberculous abscesses. Tuberculosis of the liver is often accompanied by other changes in the organ, such as congestion, fatty degeneration, amyloidosis, and fibrosis. So long as the process is restricted to the inside of the liver there are rarely any definite symptoms. The liver is sometimes moderately enlarged, and very exceptionally a tuberculous mass may be large enough to be palpable during life. Jaundice is uncommon.

## TUBERCULOSIS OF THE PANCREAS

Tuberculosis of the pancreas is relatively uncommon and probably is never primary. It is usually observed as a part of generalized tuberculosis, especially in children, the bloodvessels being the channels of infection. Occasionally, however, the pancreas becomes involved by the direct extension of a tuberculous process in contiguous lymph-nodes, the peritoneum, or the kidney. As a rule, the disease appears in the form of miliary tubercles. Caseous masses of various sizes also occur, although microscopic examination usually shows that such masses involve lymph-nodes adjacent to or imbedded in the pancreas rather than the pancreas itself. The lesions have rarely any clinical significance.

## TUBERCULOSIS OF THE PERITONEUM

Although tuberculosis of the peritoneum may rarely, perhaps, be primary, in the vast majority it is undoubtedly secondary to a focus of disease elsewhere in the body. This focus, which can usually, but not always, be demonstrated, is most frequently in the intestine, the appendix, the mesenteric lymph-nodes, or the Fallopian tubes, but it may be in the lungs or pleura, or some other structure situated without the abdominal cavity. Evidences of peritoneal involvement are found at autopsy in from 10 to 15 per cent. of all tuberculous subjects. The infection may be hemogenic, as

when it occurs as a part of a generalized miliary disease, or it may be lymphogenic or by direct extension. Occasionally it depends upon the direct introduction of bacilli into the peritoneal cavity, as when the bowel is perforated by a tuberculous ulcer or a tuberculous lymph-node undergoes disruption, although such accidents are more likely to be followed by some form of septic peritonitis.

Tuberculosis of the peritoneum is most frequent in adults between the ages of 20 and 40 years and in children between the ages of 2 and 6 years. Among adults, it is more common in women than in men (2 to 1), this disproportion in favor of females being probably due to the activating influence of parturition on tuberculous processes generally and also to the relative frequency with which tuberculous lesions occur in the Fallopian tubes. It seems to be established that traumatism may sometimes act as a predisposing factor, and that in children the acute infections, especially measles and whooping cough, favor to some extent the occurrence of the disease. It is noteworthy that tuberculous peritonitis is not an infrequent concomitant of cirrhosis of the liver.

The nature of the lesions varies with the manner of infection, the resistance of the tissues, and the stage of the process. Localized and diffuse forms of the disease are observed. The localized form usually results from the direct propagation of the infection from an intestinal ulcer to the visceral peritoneum immediately beneath it and may appear as a small group of miliary tubercles or as a solitary band of adhesions uniting more or less firmly two coils of intestine together or a coil of intestine to some other structure. Diffuse peritoneal tuberculosis frequently takes the form of a disseminated miliary disease, characterized by an abundant eruption of small tubercles, with more or less inflammatory exudation. The latter most often consists of clear serum (*ascitic type*), but it may be serofibrinous, hemorrhagic or even purulent. Occasionally in serofibrinous peritonitis collections of fluid become localized by bands of adhesions or coils of adherent intestine, and thus have the appearance of intra-abdominal cysts. In other cases the exudation, though mainly fibrinous, is interspersed with large cheesy masses formed by the coalescence of many tubercles (*so-called ulcerative* or *caseous type*). Such cheesy masses may eventually become calcified or through softening be transformed into tuberculous abscesses. The latter occasionally rupture into the bowel or discharge their contents externally through some part of the abdominal wall, usually the umbilicus. In still another form, which is essentially chronic, the abdominal contents are matted together by numerous dense fibrous adhesions (*adhesive or fibrous type*). In this form ascites may be, but is not, usually, present and there is little tendency to caseation.

The **symptoms** are variable; indeed, the condition may be entirely latent and discovered only at autopsy or at operation. In some instances the course is acute or subacute and marked by abdominal pain, tenderness and distention, with a remittent febrile temperature and gradual wasting, the clinical picture strongly suggesting typhoid fever or acute appendicitis. As a rule, however, the disease develops insidiously and pursues a more or less chronic course. In many cases increasing weakness and emaciation, impairment of appetite, and enlargement of the abdomen are the earliest manifestations. The abdominal distention may be due to an accumulation of fluid or to tympanites or to both of these conditions combined. In children, especially, the contrast between the swollen abdomen and the emaciated trunk and limbs is sometimes very marked. The fluid may move freely from one part of the abdomen to another or it may be encysted. It is

usually clear and pale amber-colored or blood tinged, but occasionally it is turbid from the presence of pus. The quantity is often moderate. Distention of the superficial abdominal veins is occasionally observed. Inflammatory changes about the umbilicus may occur. Palpation not rarely reveals a peculiar doughiness of the abdomen or even distinct tumor-like masses, the latter consisting of adherent coils of intestine, thickened and contracted omentum, enlarged lymph-nodes or encapsulated fluid. Pain and tenderness may or may not be present. In many cases, but by no means in all, there is moderate fever of a regular or an irregular type. Leucocytosis is the exception rather than the rule. Diarrhea is sometimes present, but it is usually caused by intestinal ulceration. Nausea and vomiting are not uncommon in the later stages of the disease. Jaundice, due to compression of the bile-ducts by tuberculous lymph-nodes or adhesions, has been noted in a few instances. In the fibrous or fibrocaseous form of peritoneal tuberculosis the most conspicuous symptoms may be those of chronic intestinal obstruction the consequence of compression or kinking of the bowel by adhesions (see p. 482). If the bladder is encroached upon by adhesions, frequent and painful micturition may also be a prominent feature.

The **diagnosis** is often difficult. The presence of other tuberculous lesions is of great importance and therefore careful examination should be made of the lungs, accessible lymph-nodes, Fallopian tubes, testes, etc. A history of previous pleurisy is suggestive. In children the presence of ascites without effusion in other serous cavities should always arouse suspicion, as in early life this condition is most frequently caused by tuberculous peritonitis. Cytologic examination of the ascitic fluid, if it is available, is of assistance, a preponderance of lymphocytes being in favor of tuberculosis. In doubtful cases valuable information may also be gained from the special tests and from animal inoculation.

The conditions with which generalized peritoneal tuberculosis with serous exudation is most likely to be confused are ascites from cirrhosis of the liver, multiple serositis, and malignant disease of the peritoneum or mesenteric lymph-nodes. Encysted tuberculous peritonitis has not rarely been confused with ovarian and other intra-abdominal cysts. The diagnostic features of *cirrhosis* of *the liver* are discussed on p. 529. It must be borne in mind that tuberculosis and cirrhosis are frequently coincident. In *multiple serositis* there are no indications of active tuberculosis elsewhere in the body, although there may be evidences of chronic pericarditis or pleurisy; masses of omental or intestinal tissues are never detected on abdominal palpation; the ascites is usually excessive, necessitating repeated tappings and recurring rapidly after removal; and the patient may remain in comparatively good health for a long period, sometimes many years. The diagnosis of *malignant disease* of *the peritoneum* is difficult when no primary focus can be found. In doubtful cases fever points to tuberculosis, but a hemorrhagic exudation is more in favor of malignant disease. The special tests and an examination of the ascitic fluid may be of value.

The **prognosis** must always be guarded, although remissions lasting months or even years sometimes occur and complete recoveries under medical or operative treatment are by no means uncommon. Except in infants, the prognosis is, generally speaking, more favorable in children than in adults. In infants less than one year old the disease is usually a part of a generalized tuberculosis and is almost invariably fatal. The outlook is much better, as a rule, in the ascitic and dry adhesive forms than in the caseous and ulcerative. In the pure fibroplastic type spontaneous healing is not uncommon. The presence of active tuberculosis elsewhere in the body, persistent fever, pro-

gressive emaciation, and diarrhea are unfavorable features. The danger of dissemination is, of course, always present and relapse after apparent cure is not exceptional.

**Treatment.**—All the measures that have been found of service in the treatment of pulmonary tuberculosis (see p. 59) should be employed in tuberculosis of the peritoneum. Abundance of fresh air, appropriate food and rest in bed are imperative. Sun baths have been especially recommended. In ascitic cases if the patient does not improve in a few weeks under medical measures surgical intervention should be advised. The best operation is celiotomy with evacuation of the fluid and removal of the immediate source of the infection if this is found to be in the Fallopian tubes, the ileocecal coil, or the appendix. Drainage should not, as a rule, be employed as it is likely to result in a fecal fistula. Although celiotomy itself is followed by a considerable proportion of cures (probably 40 to 50 per cent. in well selected cases) its mode of action is not definitely known. Bircher[1] in 1907 collected 1295 surgical cases and found that 31 per cent. of the patients were well after a year or more, although in 69 per cent. there had been an immediate cure. A second operation may be indicated if relapse occurs. In the fibrous or fibrocaseous form operation is inadvisable except for the relief of special conditions, such as intestinal obstruction, abscess formation, or large sacculations containing fluid.

## Tuberculosis of the Genito-urinary System

### Tuberculosis of the Kidneys

Tuberculosis of the kidneys is probably always secondary to a focus of disease elsewhere in the body. It is most frequently observed in young adults although persons over 40 are by no means immune. In children the renal involvement is usually a part of a generalized tuberculosis. Males are more commonly affected than females. Two forms of the disease may be recognized—the acute (miliary) and the chronic.

Small miliary tubercles are regularly present in the kidneys in cases of the generalized disease, and a few are frequently found after death in one or the other kidney in cases of chronic pulmonary tuberculosis, the infection in this instance probably being a terminal event and occurring also by way of the circulating blood. These types of miliary tuberculosis have no special symptomatology.

In chronic renal tuberculosis it is possible that the infection may sometimes reach the kidneys by way of the ureters (urogenous infection) from a focus in the lower part of the genito-urinary tract, although it is now generally accepted that in the vast majority of cases the bacilli reach the kidneys by way of the blood stream (hematogenous infection) and that for a comparatively long period the infection is frequently unilateral. According to Israel[2] the healthy kidney is more often infected directly from the tuberculous one than from any other focus. While chronic renal tuberculosis is rarely, if ever, primary, the initial lesion is frequently insignificant, or at least very much less conspicuous than that occurring in the kidneys. Three types of the disease may be recognized. In one type the tuberculous process begins at the apices of the papillæ and is characterized by caseous ulceration extending inward toward the cortex. In another type the organ is studded with tuberculous nodules of various sizes, which show little tendency to caseation. In the third type, which is by far the most common, a grayish nodule appears at the junction of the cortex and medulla and usually at one

[1] E. Bircher: Die chronische Bauchfelltuberkulose, Aarau, 1907.
[2] Folia Urologica, 1911, vi.

or the other pole of the kidney. This nodule gradually enlarged and becomes caseous, and ultimately the entire organ may be transformed into an agglomeration of cysts, separated from one another by septa of renal tissue and filled with yellowish-white creamy material. Occasionally the process comes to a standstill and then the caseous areas are converted into mortar-like masses by infiltration with lime-salts.

In these chronic forms of renal tuberculosis the kidney may or may not be enlarged. A variable amount of fibrosis is usually present. Mixed infection is likely to occur and therefore pus is generally found in the urine. The inflammatory process sometimes extends to the tissues around the kidney, leading to fibrous thickening of the fatty capsule or paranephric abscess. The ureteral walls frequently become thickened and ulcerated. Eventually strictures may form as a consequence of cicatricial contractions. If the ureter becomes completely occluded a closed pyonephrosis ("autonephrectomy") may result and be followed by a symptomatic cure. According to Braasch[1] renal occlusion occurs in about 10 per cent. of the cases. Sooner or later the bladder also becomes involved in the tuberculous process. In males coincident tuberculosis of the prostate and seminal vesical is extremely common (Braasch).

**Symptoms.**—In at least two-thirds of the cases the first and by far the most prominent symptoms throughout the entire course of the disease are those referable to the bladder. Increased frequency of urination (pollakiuria) and the passage of pale, slightly cloudy urine most frequently mark the apparent onset of the affection. Pain before, during, or after micturition may also be an early feature. These vesical disturbances are not necessarily due to any lesion of the bladder itself and often continue with remissions or exacerbations for a long period before any symptoms arise that point directly to the kidney. Less frequently hematuria or renal pain, varying inintensity from a dull ache to crises simulating those produced by the passage of a calculus, is the first symptom to attract attention. In the early stages the general health may be fairly good, but sooner or later weakness and emaciation supervene. The temperature is usually normal or only slightly elevated at night, unless there is mixed infection with retention of pus or a general dissemination of the tuberculous process, and then irregular fever with sweats and chills are likely to be present. Subcutaneous edema and retinal changes are rarely observed, but in advanced cases extreme weakness with nausea and vomiting may supervene as evidences of renal insufficiency. Pigmentation of the skin may occur if the suprarenal glands become involved.

Once the disease is well established variable amounts of pus and of albumin appear in the urine, and also, as a rule, tubercle bacilli. Although the latter are occasionally found in the urine of tuberculous patients even when the kidneys, bladder and genital organs are not infected, their presence in association with pus or blood is highly significant. On the other hand, pyuria without demonstrable bacteria of any kind, either by smear or culture, is equally suggestive of tuberculous infection. Tenderness, especially at the costovertebral angle is often present and in some cases there is distinct enlargement of the affected kidney. With early occlusion of the ureter a large pyonephrosis may develop. Occasionally ureteral thickening may be detected by vaginal or rectal examination. Even in the early stages cystoscopy may afford valuable information, the nature of the process often being revealed by alterations in the shape of the ureteral orifice and by inflammatory edema, ulcerations, or miliary tubercles in the mucosa around the orifice. Catheterization of the ureters, with a chemical, microscopic and

[1] Jour. Amer. Med. Assoc., Nov. 13, 1920.

bacteriologic examination of the collected urine, is very useful, not only in demonstrating the presence of renal infection, but also in determining whether one or both kidneys are involved. The various functional tests afford another means of localizing the disease and also of ascertainnig the relative efficiency of each kidney. Radiographic evidence of renal tuberculosis may be obtained in about 20 per cent. of the cases (Braasch and Olden). Abscesses in communication with the pelvis of the kidney and strictures of the ureter are sometimes clearly shown in roentgenograms after ureteral catheterization and the injection of an opaque medium (collargol or a 20 per cent. sol. of sodium bromid). The disease lasts from few months to many years, and is not rarely marked by long remissions or periods of actual latency.

**Treatment.**—Nephrectomy is the only effectual treatment and is indicated in unilateral cases unless extensive lesions are present elsewhere in the body or there are evidences of generalized tuberculosis. The earlier it is done the better are the prospects of cure. According to Wildbolz[1] of 316 cases treated by means other than surgical 70 per cent. died within 5 years and in only 5 per cent. had all the symptoms disappeared. On the other hand in the experience of Israel, Rovsing, Mayo, and others early nephrectomy is followed by marked improvement or actual cure in at least two-thirds of the cases. The operative mortality in skilled hands is less than 2 per cent. Tuberculosis of the bladder is usually improved by nephrectomy and in some cases is permanently arrested. In bilateral renal tuberculosis surgical treatment is indicated only when one organ is extensively diseased and the other is slightly involved. General therapeutic measures are important and should be continued even after operation.

## TUBERCULOSIS OF THE BLADDER

Tuberculosis of the bladder is observed chiefly as a part of a urogenital tuberculosis, being usually the result of an ascending infection from the epididymis or testicle or, as is more frequently the case, of a descending infection from the kidney. Only in rare instances is it directly secondary to pulmonary tuberculosis. The wall of the bladder may be invaded by miliary tubercles or it may become thickened and then ulcerated. The region of the ureteral orifices or of the trigonum is the favorite site. The symptoms are those of cystitis with bacilluria. Cystoscopy is a valuable aid to diagnosis.

## TUBERCULOSIS OF THE MALE GENITALIA

Tuberculosis of the male genital organs is not uncommon between the ages of 20 and 40 years. The epididymis is the part usually first affected, although a tuberculous focus is nearly always present elsewhere in the body. From the epididymis the disease may spread to the testicle or along the vas deferens to the seminal vesicles, the prostate, the bladder, etc. At the Mayo clinic 73 per cent. of 234 male patients with renal tuberculosis showed, coincident tuberculosis of the genitalia (Braasch).[2] The lesions are often unilateral, at least for a time. The symptoms consist of sexual erethism, pain on ejaculation, prostration after intercourse, and ultimately sterility and impotence. Pus may be absent from the urine in the early stages, especially if the lesions are limited to the epididymis and testicle. Tubercle

[1] Correspondenz-Bl. f. Schweiz. Aerzte, 1911 XLI, No. 36.
[2] Amer. Jour. Med. Sci., Jan., 1920.

bacilli are sometimes present in the semen or prostatic secretion, and it is possible that some cases of tuberculosis of the female genitalia have this source. Genital tuberculosis not infrequently gives rise to tuberculous meningitis or to general miliary tuberculosis.

## TUBERCULOSIS OF THE FEMALE GENITALIA

**Tuberculosis of the Fallopian Tubes.**—Of the three reproductive organs—the Fallopian tubes, the ovaries and the uterus—the first are by far the most frequent site of tuberculosis. The infection is usually secondary by way of the blood or to an entero-peritoneal tuberculosis, but it may be primary from without, the semen in some instances probably being the medium of transmission. As a rule, both tubes are involved. Williams[1] differentiates three types—miliary, chronic diffuse tuberculosis, and chronic fibroid tuberculosis. The symptoms are not distinctive, but are those of ordinary tuboövarian disease. Tubercle bacilli are sometimes present in the vaginal discharge or in particles removed from the uterus by curettage. In women tuberculous peritonitis and tuberculous salpingitis not infrequently coexist and in some instances it is difficult to determine which condition is primary and which is secondary.

**Tuberculosis of the ovary** is probably always secondary, the source of infection being the blood (general miliary tuberculosis) or, far more frequently, the Fallopian tube or peritoneum. In the majority of cases both ovaries are affected. Miliary tubercles may appear within the gland or upon its outer surface, or there may be diffuse lesions with caseation or an abscess. Occasionally ovarian cysts become tuberculous.

**Tuberculosis of the uterus** is most frequently due to a descending infection from the Fallopian tubes, but it may be the result of hematogenous infection, and in some instances it is probably primary, infection occurring by way of the vagina. The endometrium is the part usually affected.

According to W. J. Mayo[2] the tuberculosis is usually found in children before puberty or in women after the menopause and rarely occurs in menstruating uterus. The disease may take the form of discrete miliary tubercles or of a diffuse infiltration with caseation. In the cervix the condition is likely to be mistaken for carcinoma or syphilis.

**Tuberculosis of the Mammary Gland.**—Tuberculosis of the breast is comparatively rare and is probably never primary. It constitutes from 0.5 to 1.0 per cent. of all chronic breast lesions (Durante and MacCarty, Gatewood).[3] The infection may reach the gland through an abraded surface or through the milk ducts, through the blood, or through contiguity of tissue (bone disease), but in most cases, it apparently gains entrance through the lymph-channels (retrograde embolic process) from the thoracic cavity or the lymph-nodes (axillary, cervical, etc.). Two forms of the disease may be recognized: the nodular and the diffuse. Softening of the foci with the formation of sinuses is a frequent event. In the majority of cases the axillary lymph-nodes are more or less involved. The condition is likely to be mistaken for carcinoma. The treatment consists in complete removal of the breast itself and of the affected lymph-nodes.

[1] Johns Hopkins Hosp. Reports, vol. 3.
[2] Collected Papers of the Mayo Clinic, 1918, x, 147.
[3] Jour. Amer. Med. Assoc., 1916, lxvii, 23.

## Tuberculosis of the Circulatory System

**Tuberculosis of the pericardium** is less common than tuberculosis of other serous membranes, although it is by no means rare. When not a part of a general infection, it is usually secondary to tuberculosis of the pleura, lungs or mediastinal lymph-nodes. The condition may be acute or chronic, and the exudation may be serofibrinous or fibrinous, or in rare instances purulent (Kast). In the serofibrinous form the fluid is frequently blood-stained. In chronic cases the two layers of the pericardium are often greatly thickened with fibrous or fibrocaseous tissue and more or less closely bound together. In some instances the sac is completely obliterated. The symptoms of tuberculous pericarditis are similar to those of ordinary pericarditis (see p. 702).

**Tuberculosis of the myocardium** is rare and always secondary to a focus of disease elsewhere in the body, usually in the mediastinal lymph-nodes or lungs. It is more common in children than in adults. The infection may occur through the blood, through the direct extension of a tuberculous pericarditis, or by way of the lymphatics. The disease may be found (1) in miliary form, as when it accompanies acute generalized tuberculosis; (2) as large caseous nodules, single or multiple, ranging in size from a pea to a walnut; or, very rarely, (3) as a diffuse tuberculous infiltration with more or less fibrosis. Symptoms are absent or are such as may occur in other forms of myocardial disease.

**Tuberculosis of the endocardium** is even more rare than myocardial tuberculosis. It is doubtful whether more than ten of the recorded instances are genuine. The lesions, which may be in the form of miliary tubercles on the mural endocardium or of soft vegetations on the valves, are the result of a blood infection and occur only in association with generalized tuberculosis. If symptoms are present, they are those of simple endocarditis.

**Tuberculosis of the Arteries.**—The smaller arteries are sometimes involved in areas of tuberculosis, although, as a rule, they prove resistant for a long time. The cellular accumulation produced by the infection in the wall of the vessel may undergo caseous degeneration, and this, in the absence of thrombosis, may be followed by aneurysmal dilatation or rupture. It is from vessels thus affected that the profuse hemorrhages of the later stages of pulmonary tuberculosis often occur. In other cases the tuberculous process is accompanied by productive changes that result in great thickening of the arterial wall and partial or complete occlusion of the lumen of the vessel.

*Tuberculosis of the aorta* is occasionally observed. It may be due (1) to the direct deposition of tubercle bacilli upon the intima from the blood coursing over it, or, possibly, in rare instances to infection of the media by bacilli reaching this coat through the blood in the vasa vasorum; or (2) to the direct extension of a tuberculous process to the adventitia from some adjacent focus, usually a caseous lymph-node. The disease may be in the form (*a*) of a diffuse infiltration with caseation, as when it results from direct extension; (*b*) of miliary tubercles; or (*c*) of a solitary nodule projecting from the intima into the lumen of the aorta. The miliary form is usually an accompaniment of a general miliary tuberculosis which has involved the aorta and other parts almost simultaneously. The nodular form is likewise often associated with a widespread distribution of tubercles, but in this instance it is probable that the vascular lesion itself is often the immediate source of the general infection. Caseous degeneration of the coats of the aorta is a rare cause of aneurysm, as in cases cited by Kamen[1] and Tozer.[2]

[1] Ziegler's Beiträge, 1895, S. 416.
[2] Brit. Med. Jour., Dec. 12, 1914.

## Tuberculosis of the Lymphatic Tissues

### TUBERCULOSIS OF THE LYMPH-NODES

Tuberculosis of the lymph-nodes is very common, especially in childhood, which has been spoken of as the lymphoid age. The disease may be widespread, but more frequently it is regional or confined to a certain chain of nodes, especially the cervical, the bronchial or the mesenteric. The affected nodes are usually much enlarged and show a marked tendency to undergo caseation and softening, to become adherent to the surrounding tissues, and to fuse with one another, often several being united in a single tumor mass, which eventually may break down and discharge into some contiguous structure or externally. The course of the disease may be arrested, however, at any stage. Thus, in many cases the nodes after reaching a certain size become fibroid and calcareous, these changes representing an actual cure or, more frequently, a quiescent or latent stage of the infection, which may at any time, if the patient's resistance becomes impaired, break out anew.

**The Cervical Nodes.**—In tuberculosis of the cervical lymph-nodes infection usually occurs by way of the tonsils or post-nasal adenoid tissue, but it may occur by way of carious teeth, the middle ear, or the mucous membrane of the nose or throat. The infecting organisms are not rarely of the bovine type. A few nodes or the whole chain on each side of the neck may be involved. The swelling, as a rule, develops gradually and at first is not painful. It may remain for an indefinite period and then subside spontaneously, but much more frequently the nodular mass becomes adherent to the overlying skin, signs of softening and inflammation appear, and finally ulceration occurs with the discharge of caseous material and seropus. Sinuses persist for a long time and when healing ultimately occurs it is usually with irregular, unsightly scars. Of 131 cases of cervical adenitis reported by Treves[1] suppuration occurred in 93, the interval between the onset and formation of pus averaging $3\frac{1}{2}$ years.

Cervical tuberculous adenitis is, as a rule, easily recognized, but in some instances a positive diagnosis can be made only by removing a node and studying it microscopically. In *simple adenitis* due to pyogenic bacteria of low virulence the removal of the source of the infection is soon followed by resolution unless the nodular tissue has already become disorganized. *Syphilis* may usually be differentiated by the history and associated lesions. Syphilitic buboes, moreover, do not often attain the size of tuberculous nodes, rarely suppurate and are more likely to be generalized. *Hodgkin's disease* may closely resemble tuberculous adenitis, but generally it shows a predilection for the nodes in the posterior cervical triangle. The tumors, too, are painless, show no tending to break down, and for a long time are felt as discrete, freely movable masses. In doubtful cases the diagnosis may be made certain by a microscopic examination of an excised node. *Sarcoma* grows rapidly, infiltrates the surrounding tissue, is usually painful and often gives rise to metastases in various organs. In *carcinoma* careful examination generally reveals a primary growth. In *lymphatic leukemia* a systematic study of the blood will establish the diagnosis.

*Treatment.*—General hygienic and antituberculous measures should be given a thorough trial, as spontaneous recovery is by no means rare and as extirpation is completely successful in not more than 75 per cent. of the cases (Wohlgemuth, Da Costa). Carious teeth and chronic otorrhea should

[1] Scrofula and Its Gland Diseases, 1882.

always receive attention and adenoids and infected tonsils should be removed. X-ray treatment sometimes gives good results. If no definite improvement is observed after a delay of several months, complete removal of the affected nodes is advisable. It should be stated, however, that some surgeons favor a more conservative treatment and recommend that softened nodes should be gently curetted or aspirated with a small needle and then injected every third or fourth day with iodoform-glycerin. After operation medical supervision is essential. Recurrence and the development of tuberculosis in lungs or elsewhere are not rare under any method of treatment, but when the disease is limited to the upper cervical triangle a combination of medical and surgical measures usually effects a permanent cure.

**The bronchial nodes** are involved in all cases of pulmonary tuberculosis, and there is good reason to believe that in some cases, especially in children, the nodes are affected first, the bacilli reaching them by way of the lungs or the intestine without producing lesions at the point of entrance. In the majority of cases there are no symptoms or only such as may be ascribed to coexisting disease of the lungs—impairment of general health, anemia, evening rise of temperature, cough and signs of apical infiltration. If symptoms occur as a result of the adenopathy itself, they are chiefly due to pressure upon adjacent air-tubes, vessels or nerves, and are in many instances first noted after an attack of measles or whooping cough. A suggestive feature in some cases is a persistent, hard, brassy cough. Paroxysms of dyspnea, with or without a respiratory stridor, may also occur. Distinctive physical signs are rarely present. The following have been mentioned by various writers, but are by no means positive indications: Distention of the superficial veins over the chest, neck and head; weakness of the respiratory murmur on one side of the chest; paravertebral or parasternal dulness on percussion; relative dulness over and to both sides of the fifth and sixth thoracic vertebræ (de la Camp's sign); an area of tenderness in the interscapular region (Petruscky's spinalgia); well-marked whispering bronchophony in the interscapular region (d'Espine's sign); and a murmur over the upper part of the sternum when the head is retracted (Eustace Smith's sign). Somewhat more valuable information is obtained by x-ray examination. Paralysis of a vocal cord, the result of pressure upon one of the recurrent laryngeal nerves, is sometimes observed. The rupture of a softened node into the trachea or a bronchus may cause extreme dyspnea and death or may be followed by a wide-spread tuberculous pneumonia. Perforation may also take place into the pleura, pericardium, esophagus or large vessels. General miliary tuberculosis and tuberculous meningitis not rarely have their origin in tuberculosis of the bronchial lymph-nodes.

**The Mesenteric Nodes.**—Tuberculosis of the mesenteric and retroperitoneal nodes is common, and in children is often primary, the bacilli making their way through the intestinal mucosa, while this remains apparently intact. In adults the disease is generally secondary to intestinal tuberculosis. If symptoms develop they are usually due to other tuberculous lesions rather than to the infected nodes themselves. In some cases, however, especially in young children, there is persistent diarrhea with progressive weakness and emaciation and occasional attacks of fever. The abdomen is distended and usually tender on deep pressure. The stools are frequent, watery and offensive. This condition is known as *tabes mesenterica*, although in many cases the bowel and peritoneum are infected as well as the mesenteric nodes. The diagnosis is not easy, as chronic intestinal catarrh often produces a similar picture. Occasionally the enlarged nodes may be felt through the abdominal wall. Hard movable masses in the belly of a child are, as a

rule, either fecal accumulations or caseous mesenteric nodes (Branson).[1] In itself tuberculosis of mesenteric nodes is rarely a direct cause of death, and doubtless when the infection is a mild one, is often overcome. Adverse possibilities, however, are ever present, especially to be apprehended being the occurrence of tuberculosis of peritoneum, meninges or lungs and general miliary infection.

**Tuberculous Polyadenitis.**—Occasionally the lymph-nodes throughout the body are the chief seat of the tuberculous process, the viscera and other parts being but little involved. This condition, which is comparatively rare, presents a clinical picture similar to that of Hodgkin's disease, differentiation in many cases being impossible except by microscopic examination of one of the affected nodes. Of 32 cases in adults reported by Harbitz[2] the process was fatal in 30.

## TUBERCULOSIS OF THE SPLEEN

Secondary tuberculosis of the spleen is common. The lesions usually consist of small miliary tubercles, but in some instances large caseous masses are found. Occasionally the spleen appears to be the only organ affected. In these so-called primary cases there is often well-marked splenomegaly, with local pain and moderate anemia of the secondary type. Much less frequently the clinical picture is similar to that of Vaquez's disease, splenmegaly, cyanosis and polycythemia being the conspicuous features. In some instances enlargement of the liver is also present. In 1912 Winternitz[3] collected 51 cases of so-called primary tuberculosis of the spleen, 34 of which were diagnosed at necropsy and 17 at operation. Of 16 cases in which the spleen was removed, recovery occurred in 10. Six patients of the series showed polycythemia.

## TUBERCULOSIS OF THE BONE MARROW

Tubercles occasionally develop in the bone marrow in cases of advanced pulmonary tuberculosis and are nearly always present in cases of general miliary tuberculosis. The infection is hematogenic. The bone marrow may also become affected by the extension of a tuberculous process in the bone itself. So long as the lesions are confined to the interior of the bones they are without much clinical significance.

## TUBERCULOSIS OF THE DUCTLESS GLANDS

**Adrenals.**—Tuberculosis of the adrenals is important because of its relation to Addison's disease. The condition is probably always secondary, although not rarely the adrenal is the only organ in which tuberculosis is found. Miliary tubercles occur, especially in acute generalized tuberculosis, but the most frequent lesion is the chronic fibro-caseous form of tuberculosis, beginning in the medullary portion. Unless the disease is bilateral and extensive, symptoms of Addison's disease may not develop.

**Thyroid.**—Tuberculous lesions of the thyroid are rare and almost invariably secondary, the infection reaching the gland by way of the blood-stream or by extension from an adjacent structure, especially the lymph-nodes.

[1] Med.-Chir. Trans., London, 1905.
[2] Jour. Infect. Dis. 1917, 21, 196.
[3] Arch. Int. Med., 1912, ix, 680.

Goiter may or may not be present. Of 7 cases reported by Plummer and Broders,[1] all diagnosed at operation, definite signs of hyperthyroidism were present in 6.

**Thymus.**—Tuberculosis of the thymus, either in the form of miliary tubercles or caseous nodes, is occasionally observed. It is without clinical significance.

## Tuberculosis of the Bones and Joints

Tuberculosis of the bones and joints is probably always secondary, although in many cases the original focus is small and may remain quiescent. It is one of the most benign forms of the disease. The infection is hemogenic or, less frequently, by extension from an adjacent part. The majority of cases occur in childhood or adolescence. Traumatism by producing a point of lowered resistance may exert a predisposing influence. The disease usually begins in the epiphyses of the long bones and in the cancellous tissue of the small bones. The deposit of bacilli leads to the formation of tubercles and areas of diffuse granulation tissue. The Haversian canals are soon invaded and as a result there is resorption of the adjacent bone (lacunar erosion). More externally, however, where the process is not so intense the trabeculæ may become thickened at the expense of the spaces (sclerosis). Caseation, with or without softening, and fibrous hyperplasia are the succeeding steps in the lesion, the preponderance of one or the other of these changes determining the further course of the disease. Caseous degeneration results in molecular necrosis of the bone (caries) or in the death and separation of large masses of bone (sequestra). Complete softening leads to the formation of so-called tuberculous abscesses, the contents of which are puriform or cheesy. Such abscesses may break through the overlying tissues and discharge through fistulous passages or they may burrow along muscles and fascia and appear at a considerable distance from their point of origin. Thus, abscesses springing from the thoracic vertebræ often follow the sheath of the psoas muscle and appear in the inguinal region.

Sometimes a small caseous focus becomes encapsulated and healing occurs with more or less perfect motion in the affected joint. More frequently, however, the articular cartilages and bone-ends are destroyed and the process terminates in fibrous or perhaps bony ankylosis and the formation of osteophytes. Tuberculosis of the spine (Potts' disease) commonly leads to angular deformity and fixation of the vertebræ. In tuberculosis of the hip-joint there is a tendency to shortening of the affected limb. In the small bones, such as the phalanges, the medullary canal is often enlargedby erosion from within, while the shaft is much thickened by a deposition of new bone from the periosteum. This condition is known as *spina ventosa*.

While tuberculosis of the large joints is usually characterized by a diffuse infiltration of the various articular structures with granulation tissue, producing the condition clinically known as *white swelling*, the infection may be productive of nodular thickening of the synovial membrane (*synovitis tuberosa*), of serous effusion, of suppurative inflammation, or of a miliary tuberculous synovitis. According to Poncet and other representatives of the French school, the joint lesions usually classed as chronic rheumatism or arthritis deformans can also be produced by the tubercle bacillus or its toxins.

The breaking up of a tuberculous area in one of the bones or joints is sometimes followed by widespread dissemination of the infection, gen-

[1] Jour. Amer. Med Assoc. Nov. 8, 1919.

eralized miliary disease, and death. Amyloid changes in the viscera may also develop, especially if there is prolonged suppuration.

## Tuberculosis of the Nervous System

The most common and important form of tuberculosis of the nervous system is tuberculosis of the cerebral meninges. This appears as a lepto-meningitis, or more accurately, a meningo-encephalitis. Infection is usually hemogenic, but it may be by direct extension from a caseous focus in an adjacent bony structure. The membranes of the spinal cord may present similar lesions, and rarely the cord itself may be affected. The substance of the brain and cord may also be the seat of solitary or multiple tubercles. In the brain solitary tubercles (tuberculomas) occasionally reach the size of a walnut or even of a hen's egg. The symptoms of such large caseous masses are usually those of tumor.

### TUBERCULOUS MENINGITIS

Tuberculous meningitis, like other forms of meningitis, is much more common in children than in adults, the period between the second and fifth years furnishing the greatest number of victims. Young infants are not exempt, as is evident from the fact that 11 of the 52 patients treated by Koplik[1] were under one year of age. The process is probably always secondary, though in exceptional instances it appears to be primary. In every one of the 68 cases of tuberculous meningitis studied at autopsy by Weill and Pehu[2] tuberculous lesions were found in other organs of the body. The primary focus, which is often quite small and inconspicuous, is generally to be found in the bronchial or mesenteric lymph-nodes, lungs, bones, joints, middle ear, or genito-urinary tract. In many cases the meningitis represents but one of the localizations of general miliary tuberculosis. The invasion of the meninges can frequently be traced to one of the specific infections, particularly measles or whooping cough, and occasionally trauma seems to bear some relation to the occurrence of the disease.

**Morbid Anatomy.**—The lesions occur chiefly at the base of the brain, their favorite site being about the pons, optic chiasm, infundibulum, perforated spaces and in the Sylvian fissures. A variable number of discrete tubercles are seen in the meninges, particularly along the line of small arteries, and in addition there is more or less gelatinous exudation in the meshes of the pia-arachnoid. There may be very few distinct tubercles and a large amount of exudation, or *vice versa*. The walls of the arteries are almost invariably the seat of a diffuse cellular infiltration, consisting of lymphocytes, epitheloid cells and plasma cells. Not rarely this infiltration leads to occlusion of the vessels or to rupture and small extravasations. The disease commonly extends along the pia into the transverse fissure and involves the ependyma and choroid plexuses. In consequence, the ventricles are usually found dilated and filled with clear or turbid serum (*acute hydrocephalus*). The substance of the brain is always affected to a greater or less depth and in many cases the membranes of the spinal cord are also involved, especially in the cervical region.

**Symptoms.**—The disease may begin abruptly with symptoms of cerebral irritation, exactly as in the epidemic form of meningitis, but as a rule it comes on insidiously with symptoms that for a time fail to arouse suspicion.

[1] Jour. Amer. Med. Asso., April 6, 1907.
[2] Lyon Méd., Aug. 9, 1903.

The patient's disposition changes. He becomes apathetic and drowsy, and when disturbed, irritable. Sleep is fitful and frequently marked by grinding of the teeth and sudden startings. The tongue is furred, the appetite is capricious, and the bowels are constipated. Headache, worse at certain times than others, is almost invariably present. In children, it is sometimes sufficient to excite from time to time a sudden shrill scream—the hydrocephalic cry, formerly regarded as characteristic of infantile tuberculous meningitis. Such a cry, however, is by no means a constant phenomenon and moreover it may be heard in other painful diseases, particularly acute inflammation of the middle ear. Vomiting may occur at irregular intervals and without reference to the ingestion of food, but it is rarely persistent. Hyperesthesia of the skin, which is such a marked feature in other forms of acute meningitis, is frequently absent or slight and transitory in this type of the disease. The intelligence at first is usually good, but sooner or later, delirium sets in and alternates with somnolence. Convulsions, general or Jacksonian in type, are sometimes observed, more frequently, however, in children than in adults. Rigidity of the neck muscles and retraction of the head are rarely so pronounced as in cerebrospinal fever, and in many cases they are entirely absent. The occurrence of Kernig's sign (see p. 86) is also variable, especially in children. Babinski's reflex[1] can frequently be elicited and in children over 2 years of age is significant. In some cases if one hand is placed under the head and the other over the chest and the head is gently raised the legs are suddenly drawn up, the large toe ascends, and the other toes separate in a fan-like manner (Brudzinski's sign).

When the disease is fully developed the general aspect of the patient is often suggestive. The brow is contracted; the expression is vacant; the pupils are sluggish and generally more or less contracted; the conjunctivæ are slightly suffused and at times covered with a film of sticky mucus. The abdominal wall is tense and retracted, giving the belly a boat-shaped (scaphoid) appearance. Children commonly lie on the side, with the limbs strongly flexed and the fingers clenched over the thumb, which is drawn into the palm. When the finger is drawn firmly across the body a bright red line is produced, which was described by Trousseau as the tâche cérébrale, but the phenomenon is not peculiar to meningitis.

After a variable time, usually a week or ten days, the symptoms of cerebral irritation give way to those of compression. Localized pareses make their appearance, the surface becomes insensible to touch, involuntary evacuations occur, and the patient sinks into profound coma. The pareses affect chiefly the muscles of the eyes (strabismus, ptosis, dilatation and immobility of the pupils) and face, and more rarely those of the extremities. Occasionally, there is well-marked hemiplegia.

The temperature, as a rule, ranges between 99° and 102° F., and is irregular. Towards the close, however, it may be subnormal or, on the other hand, very high. The pulse at the onset is usually accelerated, but later, particularly in adults, it is often infrequent, 60, or even 50 per minute—a feature of much significance when accompanied by pyrexia. At the same time the pulse may be very irregular both in rhythm and force. The respiration, slightly hurried at first, is likely to be interrupted by sighs at the height of the disease, and to assume the Cheyne-Stokes type near the end. Changes in the fundus of the eye (swelling of the disc or optic neuritis) are present in about half of the cases, whereas in cerebrospinal fever they

[1] This consists in dorsal flexion of the toes, but more especially of the great toe, when the sole of the foot is stroked. It is found normally in sucklings.

are uncommon. Tubercles also may be seen on the choroid, but they are comparatively rare. Fluid obtained by lumbar puncture usually flows out of the cannula under pressure and in the large majority of cases is clear or but slightly turbid. If allowed to stand for a few hours it frequently presents a delicate filmy coagulum. The albumin content is comparatively high, the sugar content is comparatively low. As a rule, but not invariably, the sediment shows a preponderance of mononuclear cells and, if the examination be skillfully conducted, tubercle bacilli. Unlike other tuberculous processes, tuberculous meningitis frequently causes leucocytosis. The count, however, is usually under 20,000.

Koplik has found Macewen's sign (a hollow note on percussion of the skull over the lateral ventricles) a valuable diagnostic acid in doubtful cases of meningitis, in children beyond the age of two years. The percussion should be practiced at a point about an inch and a quarter behind the external angular process of the orbit, with the body upright and the head slightly inclined to one side. This sign occurs more frequently in tuberculous meningitis than in epidemic cerebrospinal meningitis. Before applying it, however, to the diagnosis of either form of the disease, chronic hydrocephalus and rickets with incomplete ossification of the skull should be excluded, as these conditions also yield it.

A striking feature in many cases of tuberculous meningitis is the great variation in the symptoms from day to day, marked remissions and even deceptive appearances of recovery often occurring.

**Course.**—The disease is an exceedingly grave one and for a long time was regarded as inevitably fatal, but there are on record a number of indubitable cases in which the outcome was favorable. It may run a very acute course and terminate in a few days or it may become chronic and last for several months. The usual duration, however, is from two to three weeks. It must not be forgotten that months or even years after apparent recovery the lesions may again become active.

**Diagnosis.**—A number of conditions present symptoms similar to those of tuberculous meningitis. These are other forms of meningitis, the meningismus (serous meningitis) occurring in various acute infectious diseases and in acute gastroenteritis of infancy, the meningeal type of acute poliomyelitis, cerebral abscess, cerebral tumor, delirium tremens, and uremia. In doubtful cases lumbar puncture offers the most satisfactory means of establishing the diagnosis. The diagnosis of tuberculous meningitis from other forms of meningitis is not usually difficult. The mode of onset, the course of the disease and the results of lumbar puncture are the important indices. Generally speaking, an abrupt onset, high temperature, a leucocyte count above 20,000, pronounced cervical rigidity, herpetic or other eruptions, and turbid or purulent cerebrospinal fluid containing an excess of polymorphonuclear cells are against tuberculosis. In *serous meningitis* (*meningismus*) the onset is usually more rapid, the course is shorter, and the cerebrospinal fluid throughout is free from microörganisms. In *poliomyelitis*, the onset is sudden, the meningitic symptoms are, as a rule, of short duration, and paralysis commonly appears on the second or third day.

**Treatment** is mainly palliative. Lumbar puncture often affords considerable relief, and if done every two or three days may possibly be an aid to improvement or, in very rare instances, even to recovery.

## Tuberculosis of the Skin

At least five cutaneous diseases are due to the invasion of the skin by the tubercle bacillus, namely, *lupus vulgaris*, *tuberculosis verrucosa cutis* (*post-mortem wart*), *tuberculosis cutis orificialis* (*acute tuberculous ulcer*), *scrofuloderma*, and *miliary tuberculosis of the skin*. Infection usually occurs by direct inoculation from without or by extension from an adjacent tuberculous focus, but it may be hemogenic or lymphogenic. Lupus vulgaris is a chronic condition characterized by the appearance of soft, brownish-red, papules or nodules, which either ulcerate or atrophy, leaving scars. The face is the favorite location. In the majority of cases the disease begins in in childhood or early adult life. Verrucous tuberculosis usually occurs about the knuckles and is most frequently observed in physicians, laboratory workers, handlers of hides, and others who are exposed to direct inoculation with the tuberculous virus. Orificial tuberculous ulcers are chiefly observed on the lips or corners of the mouth, and are due to infection by the secretions passing over the part. The term scrofuloderma is applied to the ulceration of the skin occurring over caseating lymph-nodes or other subcutaneous tuberculous foci. Miliary tuberculosis of the skin is rare and is observed only in association with generalized miliary tuberculosis. The lesions consist of minute papules or papulovesicles, which occasionally terminate in small ulcers.

A number of other diseases of the skin, such as lichen scrofulosorum, acne scrofulosorum, erythema nodosum, and erythema induratum, are more or less peculiar to tuberculous individuals, but their dependence upon the tubercle bacillus itself has not been demonstrated. These have been classed as *tuberculides* or *paratuberculides* and ascribed to the influence of toxins arising in distant tuberculous foci.

## Tuberculosis of the Eye and Ear

**The Eye.**—Tuberculosis of the ocular tissues may be definitely secondary to tuberculosis elsewhere in the body or it may develop in an apparently healthy person. Traumatism favors its occurrence. Of the intraocular structures the iris is most frequently involved, but all tissues of the eye, except the lens, are susceptible to infection. In many cases the cornea, sclera and uveal tract are conjointly affected.

**The Ear.**—Tuberculosis of the middle ear is probably always secondary. It is characterized by ulcerative caseous lesions of the tympanic membrane, perforation of the drum-head without pain, a scanty discharge, and rapid destruction of bone.

## Treatment of Tuberculosis

**Prophylaxis.**—The means that may be instituted by the public authorities to limit the spread of tuberculosis include: The dissemination of information concerning the prevention of the disease; the supervision of schools, tenement houses, factories, public conveyances, etc.; the systematic inspection by skilled veterinarians of dairies and slaughter-houses with the view of declaring unmarketable the milk and meat of tuberculous animals; the suppression of promiscuous expectoration in public places; the prohibition of common drinking cups; the establishment of special hospitals and dispensaries for the indigent suffering from tuberculosis; the thorough disinfection of contaminated rooms; and the compulsory registration of phthisical patients.

Tuberculous patients should be taught to hold a cloth before the mouth when coughing and to expectorate only into proper receptacles containing a disinfectant solution (5 per cent. carbolic acid) or into moistened rags or paper napkins, that should be deposited in paper bags and burned before the sputum becomes dry. They should sleep alone. Their rooms should be sunny, well ventilated, and kept scrupulously clean. Consumptives must not be kissed on the lips. The marriage of tuberculous patients should be discouraged unless the disease has been completely arrested and symptoms have been absent for at least a year, or preferably for two years. Under no circumstances should a tuberculous mother be permitted to suckle her offspring and the contact of infants with tuberculous parents should be avoided as much as possible.

Persons with a predisposition to tuberculosis can do much to increase their powers of resistance by strict attention to hygiene. Fresh air, a healthy residence, an outdoor occupation, the wearing of warm clothes, with flannel next to the skin, a diet of wholesome and nutritious food, temperate living, systematic exercise and daily sponging followed by friction of the skin are the factors to be relied upon in attempting to overcome individual susceptibility. Persons recovering from such diseases as pleurisy, bronchopneumonia, whooping-cough, measles and influenza should be treated with the utmost care. As enlarged tonsils, adenoid growths, and other obstructions in the upper air-passages interfere with free respiration and increase the risk of infection, they should be removed. Finally, all local foci of tuberculosis such as frequently appear in the cervical lymph-nodes, joints and bones, should receive immediate attention.

**Sanatorium treatment** is not indispensable, but it has a great advantage in that it permits of constant medical supervision of the patient. The sanatorium may be located in almost any climate, even within a few miles of a large city, the only requisites being moderate elevation, well-drained soil, abundant sunshine, and protection from strong winds. The chief elements of the treatment are fresh air by day and night, abundance of good nourishing food, and rest or regulated exercise. In summer not less than ten or twelve hours and in winter not less than six or seven hours should be spent out-of-doors. In Falkenstein the patients remain out-of-doors in their chairs from 7 to 10 hours a day all the year round, despite fog, rain or snow and even with the thermometer at 12° C. below zero. Of course they are sheltered from the wind and rain, and are well-covered with blankets or fur robes. The bed-room windows must be kept open during both winter and summer. As a rule, patients soon accustom themselves to live in a low temperature without discomfort.

When digestion is good the patient may be given an ordinary diet of wholesome food and encouraged to eat as heartily as his digestive powers will permit. Milk, eggs, beef, mutton, fish, fowl, fresh vegetables, cereals and fruits are suitable forms of nourishment. Pastry, fried foods, coarse vegetables, and sweets should be forbidden. As a rule, the meals should be given more frequently than in health. Thus, before rising the patient may take hot milk, cocoa or gruel; at breakfast—beef-steak, chops, fish or eggs and bacon, bread and butter, and coffee or milk; at the mid-day meal—soup, fish, meat and vegetables, salad and simple pudding or fruit; at supper—cold meat, bread and butter, cocoa and fresh or preserved fruit; at bedtime, a glass of hot milk or an egg-nog. If a sufficient amount of varied food cannot be taken to bring about a gain of from 1 to 2 pounds per week in the body weight, the daily dietary should be made to include from 3 to 4 pints of milk and from 4 to 6 eggs (raw or cooked). The extra nourishment

is best given, as a rule, between meals and on going to bed. If necessary, the milk and eggs may be variously flavored and may be discontinued for a day or two from time to time. Fats—cream, butter and olive oil—if well borne, are valuable. Cod-liver oil, though less used than formerly, is also of service. It is best given two hours after a meal, and at first the dose should not exceed a teaspoonful. Digestive disturbance and high fever are contra-indications. In every case both the diet and the quantity of food must be controlled by the patient's digestive power and weight. A diet containing more than 3000 calories is not required and may actually prove harmful. Occasionally, anorexia is so pronounced that forced feeding is necessary, but usually the patient can be persuaded to eat, especially if the food is presented to him in an appetizing form. Under the influence of fresh air and rest the appetite often returns with remarkable rapidity.

If the disease is active, that is, if the temperature at any time of the day is above 99.5° or 100° F., if the pulse-rate exceeds 90 per minute, or if the body-weight is decreasing rest is imperative. If the patient is not sufficiently ill to be kept in bed, he may lie for most of the day on a couch in the open air, warmth being maintained by abundant covering and, if necessary, by a hot stone placed at the feet. Under any circumstances absolute rest for a few weeks at the beginning of treatment is advisable, and rest for half an hour before and after meals should always be insisted upon, when it is possible. As soon as the disease becomes inactive graded exercise in the open air is indicated. Except for vigorous patients walking, first on the level and later up inclines, is the safest form of exercise. In many cases, however, calisthenics and various sorts of light out-door work may be permitted. Whatever its form, exercise should always stop short of causing exhaustion and must be lessened or abandoned if it causes fever or undue acceleration of pulse, or if it impairs the appetite.

A few weeks' residence in a sanatorium is of value even if it only serves to train the patient in the ways of the open-air treatment, but lasting benefit is rarely secured in less than three months and, except in very early cases, permanent arrest should not be expected in less than two years.

**Climatic Treatment.**—Since the open-air treatment of tuberculosis has been shown to be about equally successful in nearly all localities, a change of climate has become a matter of secondary importance. Still, there are some patients, with ample means at their disposal, to whom a protracted stay in a sanatorium would become irksome and distasteful. For such patients prolonged residence in a favorable climate is often of great value. The requisites of a suitable climate are purity of atmosphere, an abundance of sunshine, a dry porous soil, and freedom from high winds and dust. The age of the patient, the extent and type of the disease, and the condition of the other organs must be carefully considered in deciding the questions of altitude, of temperature, and of humidity. Other matters that should not be overlooked in choosing a locality are wholesome food in abundance, good accommodations, and available medical advice. Many young persons, with considerable constitutional vigor, who have but a small area of lung involved do as well in high altitudes, such as are found in Colorado, Wyoming and Montana, and in Switzerland (Davos, Arosa, St. Moritz). Other patients in the early stages seem to do better in resorts at moderate altitudes (1500 to 2500 feet) such as those of the Adirondacks, Asheville and the Muskoka region. Patients with cardiac disease, pronounced emphysema, diabetes or nephritis, and persons of advanced age are unsuitable for high altitude. Tuberculous patients who are elderly, who have advanced lesions, who exhibit pronounced constitutional irritability, or who have emphysema or

cardiac, nephritic or arthritic complications do better, as a rule, in mild climates and at low levels, for example at resorts of Southern California or Southern Arizona in this country, or at the Madeira Islands, Algiers, etc., aboard.

A change of climate is usually contraindicated in acute forms of the disease and in advanced cases of chronic tuberculosis with pronounced symptoms of secondary infection.

**Home Treatment.**—The majority of tuberculous patients are unable to avail themselves of the advantages afforded by a stay in a sanatorium or by residence in a salubrious climate. These may be consoled by the fact that many cases do well at home when the conditions are not too unfavorable. Treatment at home should be made to imitate as closely as circumstances will permit that which is followed in the sanatorium. The airiest and sunniest room should be selected for the patient. So long as he has fever absolute rest should be insisted upon. During the day, if the weather be clement, he should rest on a couch or in a reclining chair in the open air for from 6 to 10 hours, according to the season, and at night sleep with the windows open. As much nourishing food should be supplied as the digestive capacity of the patient will allow. Much stress should be laid on the danger of reinfection, and the patient urged to avoid soiling his hands or clothes with sputum, and always to wash his hands and lips before eating.

**Heliotherapy.**—Exposure to the rays of the sun apparently has a curative action and excellent results have been reported, especially in tuberculosis of bones and joints, from exposing the seat of lesion and also other parts of the body to the direct rays and rays reflected from large mirrors placed near the patient.

**Artificial Pneumothorax.**—With a careful selection of cases and proper technic, compression and immobilization of the affected lung by the method of Forlanini, which consists in introducing warm nitrogen, oxygen, or sterile air into the pleural cavity, sometimes gives good results. It may be employed in moderately or far-advanced cases in which improvement has not occurred under ordinary methods of treatment and in cases of uncontrollable hemorrhages. The chief contraindications are extensive involvement of both lungs, pleural adhesions or effusion, and serious complications of any kind, especially cardiac or renal disease. As pneumothorax therapy requires close and almost constant observation of the patient its use should be confined, as a rule, to the hospital or sanatorium. The inflations are made at first every few days and later at intervals of two or three weeks, not more than 500 or 1000 c.c. of gas being introduced at the beginning of the treatment. The gas is not allowed to flow in until free oscillation of the manometer indicates that the needle is in the interpleural space. The compression is maintained for from 1 to 2 years, and then the lung is allowed slowly to expand. The operation itself is not always successful and pleural effusion, gas embolism, pleural shock, and cardiac dilatation are among complications that may occur.

**Medicinal Treatment.**—Tuberculin is a useful adjuvant to other measures in certain cases, particularly those in which the general nutrition is good and the fever is slight. Contraindications are rapid emaciation, high temperature, active pleurisy, heart or kidney lesions, diabetes, and epilepsy. Hemoptysis and intercurrent infections call for suspension of the injections for a time. No matter which tuberculin is selected, the initial dose should be small—$\frac{1}{10,000}$ mg. of old tuberculin (O. T.) or tuberculin residue (T. R.). The injections should be given at first once or twice a week, the dose being gradually increased, but never large enough to cause a reaction, not even a

slight rise of temperature. The maximum dose varies with the individual. With O. T. it may be as high as 1000 mg. or as low as a few hundredths of a milligram. Of T. R. the final dose may reach 10 mg. or more. If evidences of increasing sensitiveness appear the injections should be discontinued for a time and then resumed with smaller doses. As a rule, it is not advisable to administer tuberculin to ambulant patients unless their tuberculosis is of the more chronic or localized form.

Creosote is often useful when the expectoration is copious and purulent. The dose should be cautiously increased from 1 to 2 minims to 10 minims three times a day. Gastric irritation and nephritis are contraindications to its use. Creosote carbonate and guaiacol carbonate are free from the disagreeable odor and taste of creosote itself and appear to be equally efficacious. Arsenic in small doses over a long period is sometimes a valuable stimulant to nutrition. Iron is of service only when there is pronounced anemia. Nux vomica may often be given with advantage. Alcohol is not usually indicated, but sometimes in advanced cases whiskey, brandy or champagne is of benefit in stimulating the appetite and lessening tissue waste. Calcium hypophosphite and other salts of calcium have been extensively employed as general tonics, but are of doubtful value.

**Treatment of Symptoms and Complications.**—*Cough* that is effectual in removing accumulated secretions from the respiratory passages should be encouraged rather than checked. Morning cough, if accompanied by very viscid sputum, may be made easier by the administration of hot water, containing a small amount of sodium bicarbonate or aromatic spirit of ammonia. Expectorants in the form of syrups should be avoided. Ammonium chloride, terpin hydrate, and the creosote derivatives may favorably influence both the cough and the expectoration when attacks of acute bronchitis supervene. Irritable, dry cough may often be controlled by discipline, the patient being trained to overcome the desire to cough by his own volition. Rest in bed and regulation of diet are valuable aids. In early cases the application of a small blister over the affected area frequently affords relief. Lozenges containing gelatin, Iceland moss, acacia, etc., with menthol are worthy of trial. Inhalations are often very effective. They may be given by means of a perforated mental inspirator, fitted over the nose and mouth, containing a sponge upon which the volatile drug is placed. A mixture of equal parts of creosote, spirit of chloroform and alcohol is suitable for the purpose. The following is another useful combination:

℞. Spiritus chloroformi.....
Creosoti.....
Eucalyptol.....
Olei pini sylvestris..... āā f℥ii (8.0 mils)

Steam charged with creosote, compound tincture of benzoin or terebene is sometimes equally beneficial. The vapor may be inhaled from a paper cone fitted over the mouth of a pitcher containing boiling water and the drug. Intratracheal injections (1 per cent. of creosote or guaiacol or 2 per cent. of menthol in olive oil) may also be tried. Cough that depends upon inflammation of the pharynx or larynx calls for appropriate local treatment and that due to acute pleurisy will usually yield to strapping of the chest or to counter-irritation. Sooner or later in many cases it becomes necessary to employ internal sedatives. Of these the least objectionable are codein, heroin, spirit of chloroform and dilute hydrocyanic acid. Such combinations as the following are useful:

℞. Codeinæ sulphatis ..... gr. iv–vi (0.25–4.0 gm.)
Spiritus chloroformi ..... f℥ii (8.0 mils)
Glycerini .....
Limonis succi .....ää f℥ss (15.0 mils)
Aquæ .....q. s. ad f℥iii (90.0 mils) M.
Sig.—A teaspoonful as occasion demands.

or

℞. Codeinæ sulphatis ..... gr. iii (0.2 gm.)
Acidi hydrocyanici diluti ..... ♏. xxiv (1.5 mils)
Glycerini ..... f℥ss (15.0 mils)
Aquæ .....q. s. ad f℥iii (90.0 mils) M.
Sig.—Two teaspoonfuls from one to four times a day.

*Night-sweats* are controlled, as a rule, by rest, a constant supply of fresh air, and regulation of the diet. If necessary, the patient may be bathed at night with cool water and alcohol, or with vinegar. An ice-bag applied to the abdomen for two or three hours in the evening is also useful. If the patient is very weak it may be advisable to give him at bedtime a glass of cold milk with brandy, and small amount of some simple food once or twice during the night. Of drugs, the most reliable are atropin, 1/200–1/100 grain (0.0003–0.00065 gm.), picrotoxin, 1/100–1/60 grain (0.00065–0.001 gm.), agaric acid, 1/6–1/2 grain (0.01–0.03 gm.), and camphoric acid, 15 grains (1.0 gm.), in cachets or capsules.

*Digestive Disturbances.*—In many cases the first indication is to correct disordered digestion. No medicines that are likely to irritate the stomach should be ordered. Only the most bland and readily digestible food should be allowed. The time of eating, as well as the character of the nourishment, should be carefully revised. The various measures and drugs that are serviceable in the uncomplicated digestive disturbances are applicable here. The most potent remedies are fresh air and rest. Acute indigestion brought on by overeating is often promptly relieved by a mercurial cathartic followed by a saline. When anorexia and slow digestion are the chief features, an alkali with a vegetable bitter before meals often has a good effect. Such a combination as the following may be employed:

℞. Sodii bicarbonatis ..... ℥i (4.0 gm.)
Tincturæ nucis vomicæ ..... f℥i (4.0 mils)
Infusi gentianæ ..... q. s. ad f℥viii (240.0 mils) M.
Sig.—Tablespoonful before meals.

Vomiting that depends upon extreme irritability of the stomach frequently yields to such sedatives as bismuth subnitrate, cerium oxalate, and hydrocyanic acid, taken before meals. Emesis that is excited by cough not rarely subsides when the patient is kept in bed and put on a liquid diet. Chloroform water taken a few minutes after the meals is useful. Counter-irritation over the affected area in the lung is sometimes of service. Vomiting that is caused by ulceration of the epiglottis or larynx will call for local anesthetics—cocain, orthoform, anesthesin.

*Diarrhea.*—Diarrhea, the result of indigestion, usually yields promptly to restriction of the diet, rest, and the administration of a mild mercurial. Persistent diarrhea will demand the use of bismuth subnitrate, 20 to 30 grains (1.3–2.0 gm.), combined with opium and intestinal antiseptics—salol, bismuth-betanaphthol, or cresosote. Combinations of tannigen or tannalbin—3 to 10 gr. (0.2–0.6 gm.)—with bismuth compounds are also useful.

℞. Tannigen..... ʒss–ʒi (2.0–4.0 gm.)
Bismuthi subcarbonatis..... ʒiii (12.0 gm.)
Codeinæ sulphatis..... gr. iii (0.2 gm.) M.
Fiant chartulæ No. xii
Sig.—One powder three or four times a day.

*Hemoptysis.*—The treatment of hemoptysis is considered on page 607.

*Insomnia.*—The treatment of the insomnia coincides in many cases with that of the cough, the fever, and the night-sweats. Fresh air, rest, and regulation of the diet are valuable aids. A glass of hot milk, malted milk or cocoa may be taken just before retiring. If the feet are cold a hot foot bath at night or the placing of hot bottles in the bed will often prove effective. Drugs should be used only after other measures have failed. The least objectionable sedatives are the bromids and veronal.

*Fever.*—In many cases the fever yields to rest in bed or in a reclining chair, combined with open-air treatment. When the temperature is high cold sponging is to be recommended. Antipyretic drugs are contraindicated. If the digestion remains good no change need be made in the diet on account of the pyrexia.

*Pleurisy.*—Mild attacks of pleuritic pain are best treated by sinapisims, applications of iodine, or strapping the affected side. If the pain is severe dry cups or small blisters may be used. Internally, the salicylates are sometimes of benefit. Occasionally, morphin is necessary. The treatment of pleuritic effusion in tuberculous patients is much the same as that of ordinary pleurisy with effusion. Thoracentesis, however, is not often advisable in the late stages of tuberculosis if the effusion is only moderate and does not seriously embarrass the cardiac or respiratory functions.

*Pregnancy.*—If the patient is seen prior to the fourth or fifth month and the tuberculosis is extensive or active the uterus should be emptied at the earliest possible date. After the fourth or fifth month an expectant plan of treatment is preferable.

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## PNEUMOCOCCUS INFECTION

Acute lobar pneumonia is excited in the vast majority of cases by the Diplococcus pneumoniæ (pneumococcus) of Fränkel and Weichselbaum. This is a lancet-shaped, non-flagellate, non-motile organism, usually growing in pairs, end to end, and surrounded by a transparent capsule, which, however, is poorly developed, except in certain strains or in certain media. It stains well by Gram's method. It grows best on media containing blood-serum, but never luxuriantly, and unless frequently transplanted soon dies. Not withstanding its comparatively low vitality on artificial media, it may remain alive and virulent in sputum and in dust for a considerable period.

Four types or strains of pneumococci are now recognized, and, with the exception of Type III which is morphologically characteristic, these strains can be differentiated only by agglutination or immunity reactions. Type I is the cause of about 33 per cent. of all cases of lobar pneumonia and Type II also of about 33 per cent. Immune sera produced by each of these two types have been obtained from horses and seem to have specific therapeutic value. Type III, which was formerly classfied with Streptococcus mucosus, has a distinct capsule and produces an abundant, stringy mucous growth on surface colonies. It is the cause of from 10 to 15 per cent. of the cases of lobar pneumona. Type IV comprises a heterogenous group of pneumococci,

each number of which produces a specific agglutinin for itself. It is the cause of about 20 per cent. of all cases of pneumonia. These various types show no tendency to mutation.

Type IV is present in the mouths of nearly 2 out of 3 normal persons, but it is of low pathogenic power, the mortality of cases of pneumonia due to it not being more than 10 to 15 per cent. Type I and Type II cause pneumonia of average severity (about 25 to 30 per cent. mortality) and Type III, which is possessed of high pathogenic power, causes pneumonia with an average mortality of about 50 per cent. Types I, II and III do not occur regularly in the buccal secretions of normal persons, but are found in the mouths of patients with pneumonia, in the mouths of convalescents, and in the mouths of healthy persons who have been in contact with pneumonia patients. It is probable that infection with these three types of pneumococci is acquired usually by direct contact with an active case of pneumonia, or, more frequently, by association with a healthy carrier, although the possibility of air-borne infection in some cases cannot be entirely excluded. Infection with Type IV pneumococcus may be autogenic.

As a fairly large percentage of persons carry the organisms of pneumonia in their mouths without suffering any ill effects it is evident that some unusual condition must arise before infection can occur. This condition seems to consist chiefly in decreased tissue resistance, local or general, or the part of the host. From the cavities of the nose and throat or other portal of invasion the organisms may be disseminated by direct continuity of structure, or they may gain access to the lymph stream or circulating blood and thus be transported to organs more or less remote. Hence, infection by the pneumococcus may be local or general. In the lungs it induces various grades of reaction—active congestion of the lungs (*maladie de Woillez*), bronchopneumonia, and especially croupous or lobar pneumonia. Other tissues, chiefly the mucous and serous membranes, may be involved during the course of a pneumonitis, or without the occurrence of this localization. Thus, the pneumococcus is often the incitant of inflammation in the upper respiratory passages and contiguous structures—coryza, bronchitis, otitis media. It is the specific causative agent in many cases of pleurisy and pericarditis. Meningitis is not rarely of pneumococcic origin. As a result of blood infection it may produce endocarditis, thrombophlebitis, or arthritis. It is occasionally the only organism present in peritonitis. Finally, there may be a general blood invasion or pneumococcic septicemia, with wide dissemination of the diplococcus, but having, as a rule, pneumonitis as one of its local expressions.

## Acute Lobar Pneumonia

### (Croupous Pneumonia)

**Definition.**—Acute lobar pneumonia is the chief clinical expression of pneumococcic infection. It is a specific, self-limited disease, characterized by inflammation of the lungs, high temperature, toxemia of varying intensity, and a marked tendency to terminate abruptly by crisis.

**Incidence.**—Pneumonia is one of the most prevalent and fatal of all acute diseases, and appears to be increasing in frequency. In this country in 1870 the deaths from it per 10,000 of population were 10.24, and in 1900 they were about 14.0. In this same period other infections gradually decreased in frequency. Thus, in the mortality returns of many large cities pneumonia has advanced to the second place in the list of diseases causing death, while tuberculosis has dropped to the third place. The cause of the gain in the frequency and fatality of pneumonia is not wholly apparent, but

doubtless the increasing urban concentration, the increasing number of persons who live to be more than sixty years of age, and the prevalence of influenza in recent years have been factors of some moment.

**Etiology.**—The pneumococcus is now considered to be, with rare exceptions, the sole incitant of lobar pneumonia. In a small percentage of cases some other organism, such as the Bacillus of Friedländer, the Streptococcus pyogenes, Bacillus typhosus, or Bacillus influenzæ appears to be the infective agent. The frequent occurrence of highly parasitic pneumococci in the buccal secretions of persons who have been in contact with cases of pneumonia and the numerous records of local outbreaks in barracks, jails, hospital-wards, etc., are ample proof that the disease is to a certain extent contagious. The infection is spread chiefly by association with healthy carriers, less frequently by direct contact with active cases of the disease. Infection apparently takes place in the large majority of cases by way of the bronchi, but it is not improbable that in exceptional instances the disease may be a secondary localization of a primary blood infection. The view that the invasion may rarely be hematogenous finds support in the occasional occurrence of pneumonia secondary to pneumococcus infection in other parts of the body, and in the few cases on record of placental transmission (Netter, Ballantyne, Don, and others).

**Conditions Influencing Infection.**—*Season and Weather.*—It is universally conceded that pneumonia is most prevalent during the winter and spring months. The greatest incidence is usually observed in insular countries during December, January and February, and in inland countries during March, April and May. Although steady cold is not a predisposing factor, sudden changes of temperature, especially when the average temperature is low, seem to exercise an important etiologic influence. Climate itself plays a minor rôle.

*Residence.*—Persons living in the open country suffer less from pneumonia than those living in great cities. Even in cities the incidence is proportionately less in the sparsely settled portions than in the overcrowded districts.

*Army Encampments.*—Pneumonia often prevails to an unusual extent among new recruits in barracks and tents. This high incidence is to be ascribed to the presence of carriers, close contact in sleeping quarters, fatigue, etc.

*Age.*—Pneumonia may occur at any age. It is most frequent, however, at three periods—between the first and tenth years, between the twentieth and fortieth years, and after the sixtieth year. The period of highest mortality is between the sixtieth and eightieth years.

*Sex.*—Statistics show that males are more frequently affected than females, but the disparity in the number of cases in the two sexes is probably attributable to factors other than sex itself. In childhood boys and girls appear to be about equally susceptible.

*Race.*—Negroes appear to be more susceptible to pneumonia than the whites, although the greater fatality among the former may depend less upon racial peculiarities than upon other factors, such as poverty and irregular habits.

*Occupation.*—Persons engaged in occupations necessitating exposure to the vicissitudes of weather are more liable to the disease than those who labor indoors.

*Individual Predisposition.*—The frequent recurrence of pneumonia in the same person indicates an individual predisposition to the disease, but it does not imply necessarily that one attack favors the occurrence of others.

A history of three attacks in one patient is not very unusual. In one of Andral's patients the disease appeared sixteen times in eleven years (Eichhorst).

*State of the Health.*—Although pneumonia frequently attacks the most robust, it is more likely to occur in persons who have become enfeebled through intemperance, previous disease, unsanitary environment, excessive physical exertion, or violent psychic disturbances. The important predisposing influence of alcoholism is well recognized, as is also that of certain acute diseases, such as typhoid fever and influenza. The frequent development of pneumonia as a terminal infection in chronic disorders, especially arteriosclerosis, chronic nephritis, and diabetes, is noteworthy.

*Cold.*—The early development of pneumonia after sudden chilling of the body is a matter of such universal experience that the predisposing influence of cold must be accepted as a fact.

*Traumatism.*—The discovery of the pneumococcus has relegated injury to a secondary place in the etiology of pneumonia, but it still remains a factor. Of 3,373 cases collected by Stern, only 44, or 1.3 per cent. could be traced directly to trauma. Contusion of the thorax, even in absence of an actual wound of the parietes, seems capable of promoting infection. It is likely that the circulatory disturbances induced by the injury serve to lower the resistance of the pulmonary tissues.

*Etherization.*—The pneumonia that not rarely occurs after surgical operations in which ether has been used as a general anesthetic is sometimes lobar in type. Aspiration of pneumococci, chiefly of Type IV, with the saliva is the essential factor, but doubtless chilling of the lungs by the evaporation of the anesthetic, the irritant action of the ether itself, and the lowered resistance of the tissues resulting from the anesthesia and the operation are predisposing influences.

**Morbid Anatomy.**—Lobar pneumonia usually involves a large area of the pulmonary tissue, as a lobe or even a whole lung, in a more or less uniform manner. The lower lobe of the right lung is most frequently affected, and next to this the lower lobe of the left lung. The upper lobe of the left lung is probably the least frequent seat of the disease. Double or bilateral pneumonia occurs in from 15 to 20 per cent. of the cases. According to Ashton and Landis,[1] of 900 cases occurring in the Philadelphia Hospital between 1897 and 1904, the right lung was alone involved in 54.1 per cent., the left lung was alone involved in 32.6 per cent., both lungs were involved in varying positions in 13.3 per cent., and lesions of the apex alone, in one or both lungs, were present in 14.2 per cent. These figures correspond very closely with those of Aufrecht (1501 cases), Osler (100 cases) and Norris (500 cases). The inflammation is not always strictly limited by the lobar septa; sometimes one lobe and a part of another are affected.

Since the time of Laennec, three stages of the pneumonic process have been recognized—engorgement, red hepatization, and gray hepatization.

*Stage of Engorgement.*—The affected portion of the lung remains distended when the chest is opened. It is intensely red, less crepitant than normal pulmonary tissue, and pits upon pressure. On section frothy, blood-stained serum freely exudes. Microscopic examination reveals marked distention of the capillaries with blood and the presence in the air-cells of a few erythrocytes, leucocytes, and detached epithelial cells, together with a small amount of clear fluid (blood serum).

*Stage of Red Hepatization.*—In this stage the inflamed lung, owing to the abundance of cells in the alveoli and the coagulation of the serous exudate,

[1] Amer. Jour. Med. Sci., June, 1905.

is transformed into a solid mass resembling liver-tissue. The hepatized portion is swollen and may show the imprint of the ribs. The color is somewhat darker than in the first stage. The affected tissue is airless, noncrepitant, and friable. A torn surface is dry and granular. This granular appearance is almost pathognomonic, and is due to the projection of fibrinous plugs from the alveoli. The pneumonic lung may weigh from 1200 to 2000 grams, i.e., two or three times as much as the normal lung. It is so heavy that when an excised portion is placed in water it immediately sinks. Microscopic examination shows the alveoli to be filled with a fibrinous coagulum, enclosing within its meshes red blood corpuscles, leucocytes and a few desquamated epithelial cells. Many of the leucocytes are polymorphonuclear, although in the early stages mononuclear cells may predominate. Thrombi are frequently seen in the capillaries. Occasionally the solid exudate extends from the alveoli into the bronchioles, producing the *massive pneumonia* of Grancher. Suitable staining of pneumonic tissue usually reveals large numbers of diplococci.

*Stage of Gray Hepatization.*—The transition from red to gray hepatization is never well defined. As the process advances, however, the red color gradually gives place to a mottled gray. At the same time the tissue becomes more moist and soft. When cut and squeezed it yields a turbid fluid, rich in albumin. These changes are due partly to compression of the capillaries by the ever-increasing exudate, and partly to retrograde changes in the exudate itself. Microscopic examination reveals decolorization or complete disappearance of the red blood corpuscles, disintegration of the fibrin and extensive leucocytic infiltration, not only of the alveoli, but also of the interstitial tissue. The white cells show all grades of fatty degeneration. In this stage there is also, according to Flexner, a simple liquefaction of the exudate (autolysis), which is effected through the agency of the leucocytic enzymes. An extreme form of gray hepatization is also observed in which the cut surface of the lung is thickly coated with veritable pus. It is doubtful whether this advanced stage, to which the term *purulent infiltration* has been applied, is compatible with life.

Although it is convenient for the purpose of description to retain this classic division of the pneumonic process into three stages, it must not be supposed that these always follow one another in orderly succession. They vary widely in duration and often overlap. Not infrequently gray hepatization is found in persons dying before the third or fourth day, and sometimes red hepatization is found as late as the second or third week.

**Associated Lesions.**—The part of the lung unaffected by the pneumonic process is usually congested; occasionally it is also edematous. The bronchi are usually inflamed. In some cases the finer tubes are filled with fibrinous casts. The peribronchial lymph-nodes are enlarged. The pleura very rarely escapes. As a rule, the exudate amounts to no more than a thin deposit of fibrin over the diseased lobe, but not infrequently there is a more or less abundant serous or purulent effusion. As in other acute infections, the heart muscle and the kidneys are the seat of parenchymatous degeneration. White clots are very often found in the chambers of the heart, especially in the right auricle and ventricle. The spleen is soft and pulpy, but not often enlarged. Other localizations of the pneumococcic infection are sometimes found in the pericardium, endocardium, meninges or joints.

**Terminations.**—In the majority of cases lobar pneumonia ends in resolution. In this event the solid exudate is transformed into an emulsion by autolysis and fatty degeneration, and is then absorbed. In the fatal cases, the final outcome is usually to be attributed to failure of the circulation.

This depends in part upon direct injury to the heart by the toxins of the disease, aided, perhaps, by the mechanical impediment offered to the outflow of blood from the right ventricle by the solidified lung. There is a widespread belief that paralysis of the vasomotor center is also an important factor, but recent studies by Porter and Newburgh[1] indicate that the vasomotor reflex is not seriously impaired even in fatal cases of pneumonia. Boothby[2] suggests that the factor which regulates respiration and governs the ventilation of the lungs also governs the circulation of the blood. In many cases only trivial lesions are found post-mortem in the heart when there have been most pronounced symptoms of circulatory failure during life; moreover, the symptoms of cardiac embarrassment often disappear abruptly on the occurrence of crisis, even though the lung still remains obstructed. The chief danger undoubtedly lies in the toxemia, and the severity of this bears little, if any, relation to the extent of lung involved, but varies with the virulence of the infection and the degree of reaction in the individual attacked. Complications, principally of pneumococcus origin, such as ulcerative endocarditis, pericarditis and meningitis, are the immediate cause of death in not a few of the fatal cases. Among the unusual terminations of the pneumonic process are abscess and gangrene, the result of polymicrobic infection of the inflamed area. Ordinary lobar pneumonia probably never terminates in tuberculosis. Finally, instead of resolution occurring at the usual time there is occasionally a gradual substitution of fibrinous exudate by newly formed connective tissue derived either from the alveolar walls or the walls of terminal bronchioles. To this condition the term chronic interstitial pneumonia or cirrhosis of the lung has been applied. The studies of MacCallum and Cole and of Wadsworth[3] suggest that secondary infection may play an important part in inducing the grade of reaction necessary for organization.

**Symptoms.**—The disease usually begins abruptly with a decided chill lasting from a quarter of an hour to an hour. This is accompanied or soon followed by more or less pain in the affected side. The temperature rises rapidly, sometimes attaining a maximum of 104° F. or more in the first twenty-four hours, and continues high, with slight diurnal remissions, until the fifth, seventh, ninth or eleventh day, when, as a rule, it falls abruptly by crisis, reaching the normal within twelve hours. In about one-third of the cases the temperature falls by lysis. The pulse varies in frequency with the height of the temperature, and in favorable cases rarely exceeds 120 or 130 a minute. Though full and strong at first, it frequently becomes small and feeble as the disease advances. Cough is usually present from the beginning of the disease. It is short, painful, and partially suppressed. At first it is dry, but usually by the second or third day it is associated with characteristic reddish brown, viscid sputa. The breathing is always more or less embarrassed, and in severe cases dyspnea may be very marked. The respirations are shallow and hurried, and range from 40 to 60 a minute, thus making the ratio between the respirations and pulse 1 to 3 or 1 to 2. The face is flushed, the expression is anxious, the lips and alæ of the nose are often the seat of herpetic vesicles; the tongue is heavily furred; the bowels as a rule are constipated, and the urine is scanty, high colored, deficient in chlorids, and frequently albuminous. In many cases there is mild delirium, especially at night. At the time of the crisis the distressing symptoms speedily subside, profuse sweating occurs, and the patient falls into a quiet, natural sleep.

[1] Am. Jour. Physiol., 1914, xxxv.
[2] Am. Jour. Physiol., 1915, xxxvii.
[3] Jour. Med. Research, 1918, xxix.

In the early stage, that of engorgement, the physical signs are chiefly auscultatory and consist in a partial suppression of the respiratory murmur, and the occurrence of fine, crackling sounds at the end of full inspiration—the crepitant râles of Laennec. In the stage of consolidation the affected area yields on inspection deficient expansion; on palpation, exaggerated vocal fremitus; on percussion, pronounced dulness; and on auscultation, broncophony and bronchial breathing. The stage of resolution is marked by an abrupt or gradual disappearance of the abnormal signs of the preceding stage, and the appearance of moist râles, some of which are fine (redux crepitus), while others are coarse, and even bubbling.

**Symptoms in Detail.** *Onset.*—In the majority of cases the onset is sudden. Not infrequently, however, there is a well-defined prodromal period of several days' duration, characterized by malaise, anorexia, headache, pain in the back, chilliness and more or less severe bronchitis or coryza. A pronounced chill is the most constant initial symptom. It was present in 466 of 949 cases analyzed by Sears and Larrabee.[1] Occasionally it is preceded by pain in the side or vomiting. In children the chill is usually absent; vomiting, or more rarely, a convulsion taking its place. In rare instances the disease is ushered in with coma.

*Pain*, usually of a stabbing character, and aggravated by cough and deep breathing, is present in a large proportion of the cases in which the lower lobes are involved. It is an expression of the accompanying pleurisy and rarely lasts more than two or three days. It is often absent in children and old persons, and in apical pneumonia irrespective of the patient's age. As a rule, the pain is located in the region of the nipple or at the base of the affected lung, but in some cases, especially in children, it is referred to the abdomen and is attended with tenderness and even with rigidity, thus producing a clinical picture very like that of appendicitis, cholecystitis, or perforative peritonitis. In such cases an error in diagnosis may usually be avoided by noting the accelerated respiration, which is out of proportion to the pulse and temperature, the disappearance of tenderness on deep pressure with the flat of the hand, and the presence of cough or specific signs of pneumonia.

*Fever and Crisis.*—The temperature rises rapidly during the chill, and often reaches the maximum of 104° or 105° within the first twelve hours. During the fastigium it usually remains constant, the daily variations not exceeding 1°. In some cases, however, the temperature is distinctly remittent. Defervescence is effected by crisis in about 60 per cent. of the cases terminating favorably. This phenomenon generally begins in the evening, and is frequently completed within twelve hours, although it may require twenty-four or forty-eight hours. By far the largest proportion of crises occur between the fifth and ninth days. Exceptionally crisis occurs as early as the third day or as late as the twenty-first day. When the temperature remains high after the fourteenth day it is more likely to fall by lysis than crisis. As a rule protracted fever indicates the occurrence of a complication, particularly empyema. Sometimes a distinct rise in the temperature takes place just before the crisis (precritical rise). After the crisis the temperature may remain subnormal for several hours, or on the following day it may rise again to 99° or 100° (post-critical rise). Occasionally the fastigium is interrupted by a pseudocrisis, in which the temperature falls abruptly three or four degrees, and then rises again to its former height, where it continues until the final defervescence. The actual crisis is usually attended with profuse perspiration, and is followed almost immediately, in the vast majority

[1] Med. and Surg. Rep. of Boston City Hosp., Dec. 1, 1901.

of cases, by a marked improvement in the general symptoms, although no decided change may occur in the physical signs for several days, or, in cases of delayed resolution, for three or four weeks. Exceptionally, the crisis is followed by profound exhaustion or collapse. Death occurred after the crisis in 29 of the 949 cases analyzed by Sears and Larrabee.

In rare instances, especially in drunkards and very old persons, pneumonia runs an afebrile course.

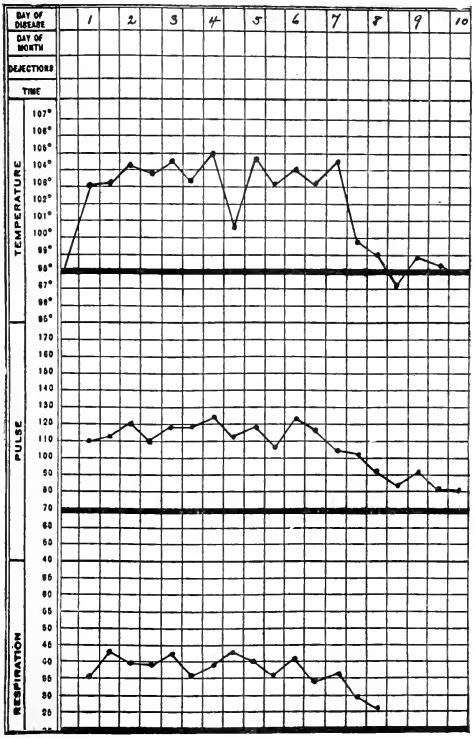


FIG. 2.—Temperature, pulse and respiration curve of an ordinary case of lobar pneumonia, showing pseudocrisis on fifth day and crisis on the eighth day.

*Respiration.*—The respirations are hurried and shallow. They resemble the panting of a dog. In adults the number may reach 40 or 50 a minute, and in children 50, 60 or even 80 a minute. Very frequently, especially in children, there is a characteristic expiratory moan or grunt. Speaking is difficult and deep breathing is painful. Dyspnea accompanies the accelerated respiration in the majority of cases. As it is disproportionate to the amount of lung involved, and disappears at the time of crisis, although the lung still remains

obstructed, it can be due only in part to the diminution in the breathing capacity. Irritation of the central nervous system by the toxins of the disease seems to be an important factor, although the pleuritic pain, high temperature, and cardiac embarrassment are not without influence.

*Cough and Expectoration.*—Cough is an early symptom. In the majority of cases, especially during the first three or four days, it is short, smothered and painful. After the crisis it is usually easier. Sometimes on the approach of a fatal termination it ceases entirely. In old and very feeble persons pneumonia may run its course without cough.

The expectoration is characteristic. For a day or two it consists of glairy mucus, then it becomes viscid, translucent, and more or less bloody. Owing to its glutinous properties the patient has much difficulty in expelling it. Although the color varies in different cases, it is usually brownish red, like that of fresh iron rust, hence pneumonic sputum is described as "rusty." After the crisis the expectoration becomes mucopurulent and more abundant. In some cases, chiefly those of a grave character, the sputum presents the appearance of prune juice. Hemoptysis, more or less pronounced, is occasionally observed at the onset. Not infrequently, especially in children and old persons, there is an entire absence of expectoration.

Microscopically the sputum contains blood cells, alveolar epithelium, pigment granules, pneumococci and other organisms, and, sometimes, fibrinous casts corresponding to the ramifications of the finer bronchi. The casts may usually be seen with the naked eye if looked for on a dark background. Chemically, the sputum is comparatively rich in protein and sodium chlorid.

*Pulse and Heart.*—In adults the pulse-rate usually ranges between 100 and 120. If it is persistently above 120 the outlook is grave. In young children, however, it is frequently between 150 and 170 even in cases of average severity. After the crisis the pulse-rate may fall to 60 or less. At the onset the pulse is often full and bounding, but as the disease progresses it tends to become small and soft. A persistently low systolic blood-pressure is usually an unfavorable sign, but there are many exceptions to Gibson's[1] rule that "when the arterial pressure, expressed in mm. Hg., does not fall below the pulse-rate expressed in beats per minute, the fact may be taken as of excellent augury, while the converse is equally true." Arhythmia at the height of the disease is an unfavorable indication.

The heart sounds are usually clear, although occasionally a soft, systolic murmur is heard over the mitral or pulmonic area. Owing to the increased resistance in the lesser circulation, the pulmonic second sound is often unduly accentuated. Dilatation of the right ventricle is manifested by feebleness of the pulmonic second sound, a small pulse, an increase in the area of cardiac dulness to the right of the sternum, cyanosis and labored breathing. In grave cases the heart-sounds may ultimately acquire the fetal rhythm.

*Cerebral Symptoms.*—It is not unusual for the mind to be clear during the entire course of the disease. Very frequently, however, there is slight delirium, particularly toward evening. In the later stages of grave cases delirium is likely to pass into stupor and coma. In drunkards the nervous symptoms may assume all the characters of delirium tremens. Occasionally, in persons not given to drink, there is violent delirium, even at the onset, the disease thus closely resembling acute mania. In other cases stupor occurs so early and is such a dominant feature that the condition is regarded as uremic. In children a convulsion may take the place of the initial chill

[1] Edinburgh Med. Jour., 1908, N. S., xiii, 17.

and other nervous symptoms, such as headache, delirium, twitching of the limbs, and stiffness of the muscles of the neck, are often so pronounced that meningitis is suspected.

Very rarely a mild form of confusional insanity develops after the crisis (post-critical delirium), persists for a few days or even a few weeks, and then disappears.

*Digestive Organs and Spleen.*—Vomiting frequently occurs at the onset, especially in children. The tongue is invariably coated. In severe cases it becomes dry and brown, and sordes collect upon the teeth. The appetite is lost. As a rule, the bowels are constipated. Tympanites is not uncommon and may add considerably to the respiratory embarrassment. It may be merely an expression of gastrointestinal disturbance, but much more frequently it is a sign of paresis of the intestinal muscle, a result of the general toxemia, and when marked is of serious significance. The frequent reference of the pain to the abdomen and the simulation of appendicitis and peritonitis by pneumonia has already been mentioned. Jaundice is occasionally present. Aufrecht observed it in 1 per cent. of 1501 cases, Norris in 3.6 per cent. of 500 cases, and McCrae in 3.8 per cent. of 465 cases. It is probably caused in most cases by a concomitant catarrh of the bile ducts, although the possibility of a hematogenous origin in some instances must be admitted. Unless severe, it is of little significance.

The liver and spleen are sometimes enlarged, the latter more frequently than the former.

*Skin.*—The surface is hot and pungent. The cheeks are flushed, the one corresponding to the affected lung often being more congested than the other. Cyanosis is sometimes noticeable, but it is rarely marked unless the right ventricle is seriously embarrassed. Herpes occurs more frequently in pneumonia than in any other febrile disease, being noted in from 25 to 45 per cent. of the cases. Ordinarily it is seated on the lips or alæ of the nose, but it may appear on other parts. This symptom has been regarded as a favorable omen, but in itself it is probably without prognostic significance. As it is especially common in young robust subjects and notably infrequent in very old persons, of course more recoveries occur among those who present herpes than among those who do not. Sweating may occur only at the crisis, but it is not very unusual at the height of the disease. A cold, clammy sweat is often observed on the approach of a fatal termination.

*Blood.*—The coagulation time of the blood is often prolonged. Slight anemia is usually present, although it may not be noticeable until after the crisis. In the large majority of cases a well-marked leucocytosis develops about the time of the chill, and persists until a few hours before or after the crisis. The degree of leucocytosis varies with the severity of the infection and the intensity of the resistance offered by the patient. The number of leucocytes usually ranges between 15,000 and 35,000 per cubic millimeter, polymorphonuclear cells making up from 80 to 90 per cent. of the total. Eosinophiles are often entirely wanting, especially in severe cases. In extremely mild attacks and in very severe ones with feeble reaction there may be no leucocytosis. Pneumococci in variable numbers are present in the blood in from 50 per cent. (Cole) to 85 per cent. (Rosenow) of the cases. High grades of bacteremia (more than 5 colonies per cm. of blood) are of unfavorable omen (Cole, Clough, Sutton and Sevier[1]). At the time of the crisis or during convalescence, blood serum tested against a homologous strain of pneumococcus usually gives evidence of the presence of protective bodies.

[1] Bull. of Johns Hopkins Hosp., 1917, xxviii, No. 320.

*Urine.*—The urine is scanty, high-colored, and of high specific gravity, and may contain a trace of albumin and a few tube-casts. The output of urea, uric acid and phosphates is increased. Special importance is attached to the excretion of chlorids, which is usually very much diminished and occasionally sometimes wholly suppressed. According to Hutchison (Jour. of Path. and Bact., Vol. V, 1898) the chlorids are retained in the fixed tissues of all the organs, but the cause of their retention is not apparent. Great diminution or absence of chlorids is of little diagnostic value, although it is probably more constant in pneumonia than in any other febrile disease. The degree to which the chlorids are reduced is no criterion of the severity of the attack.

**Physical Signs.** *Inspection.*—The respiratory movements of the affected side are usually diminished, especially after the occurrence of hepatization.

*Palpation.*—Vocal fremitus over the pneumonic lung is increased in the large majority of cases. This sign is not always apparent, however, until the patient has expelled the secretion from the bronchi by coughing. Exceptionally the fremitus is persistently diminished or absent owing to the presence of a solid exudate in the bronchi (massive pneumonia), or the development of a pleuritic effusion. Occasionally a pleuritic friction may be felt.

*Percussion.*—In the stages of engorgement and resolution the quality of the percussion note is usually tympanitic, even though the resonance may be slightly impaired. In the stage of hepatization the note is very dull, but rarely flat as in a pleuritic effusion, since a certain amount of air is still present in the bronchi. Over the unaffected portion of the lung the note is hyperresonant and more or less tympanitic. (Skodaic resonance.) Occasionally a cracked pot note may be obtained near the border of the solid area or actually over it, especially in apical pneumonia, but the cause of this phenomenon is not apparent.

*Auscultation.*—In the early stage respiration is usually feeble; less frequently it is harsh and broncho-vesicular. The chief physical sign of this stage, however, is the crepitant râle, which is heard as a rule at the close of deep inspiration, and only rarely during expiration. Although great significance is to be attached to this râle when it occurs in association with chill, pain, fever and cough, it is not pathognomonic of pneumonia, nor is it universally present in this disease. It is frequently to be heard at the lower margin of the lungs in healthy persons after they have been breathing superficially and then take deep breaths, and it may also occur in edema, infarct and tuberculosis of the lung. It is generally assumed that the crepitant râle is produced by the forcible separation of the adherent alveolar walls during forced inspiration, but Osler and Lindsay incline to the view, first advocated by Leaming, that it is nothing more than a fine pleuritic crepitus. Not infrequently larger râles, both dry and moist, accompany the fine crepitation. In many cases a coarse pleuritic friction may also be heard.

With the completion of solidification, bronchial breathing and bronchophony appear. Bronchial breathing is virtually the glottic murmur as normally heard over the trachea. Both the inspiratory and the expiratory sounds have a blowing quality, and both are prolonged, but the duration of expiration often exceeds that of inspiration. This distinct transmission of the glottic murmur to the surface of the chest is due to the obliteration of the air-spaces, which normally serve to dissipate the sound, and not to the superior conducting power of the solid lung itself. Indeed, solid lung itself is not so good a conductor as normal lung. It is not improbable that the metallic quality and great intensity of the bronchial breathing in pneumonia

may be dependent upon the reinforcement of the glottic sounds by vibrations emanating from the larger bronchi, these tubes serving as good resonators when incased in solid tissue. Bronchial breathing, however, is not necessarily loud; in many cases of pneumonia it is but barely audible. Occasionally the respiratory sounds over the hepatized area are wholly suppressed. This anomaly is probably due to blocking of the bronchi by exudation. Typical bronchial breathing sometimes develops in such cases after a paroxysm of coughing. Bronchophony, or exaggerated vocal resonance, owes its origin to the same physical conditions as bronchial breathing; hence these two signs usually appear and disappear together. Not infrequently the conditions are so favorable to the reinforcement of the voice sounds that the consolidated lung yields perfect pectoriloquy. The signs of consolidation (bronchial breathing and bronchophony or pectoriloquy) are usually obtainable within two or three days after the onset, but in some cases they do not develop until late in the course of the disease. As a rule they disappear about the time of crisis, but they may persist for several days or longer after defervescence has been completed.

As resolution progresses, the signs indicate a gradual return of the lung to its normal condition. Crepitant râles reappear (redux crepitus) and are soon followed by moist râles of various sizes; the respiration loses its bronchial character, becomes indeterminate, and finally merges into vesicular breathing; the voice sounds grow less and less intense; and the dulness gives way to impaired resonance, then, very frequently, to tympanitic resonance, and at last to normal resonance.

**Aberrant Forms.**—The course of lobar pneumonia presents many modifications. Some departures from the usual type depend upon the age, general health or individual susceptibility of the one affected, while other variations depend upon the virulence of the invading organism or the presence of other parasites, such as the streptococcus, staphylococcus, bacillus of typhoid fever or bacillus of influenza, in association with the pneumococcus. Many of the most atypical forms are the result of a mixed infection.

*Pneumonia in Infants.*—The initial chill is usually absent. In its stead there is often vomiting or, rarely, a convulsion. Pain is frequently referred to the abdomen. Cough is not a prominent feature and expectoration is seldom seen. Hurried breathing with noisy "grunting" expiration is the chief respiratory symptom in a large proportion of cases. Nervous phenomena—apathy, drowsiness, delirium, twitching of the muscles, and rigidity of the neck—are very common and simulate meningitis. The physical signs are essentially the same as in adults, although they may be unusually late in appearing. The duration is somewhat shorter than in adults, but complications, especially purulent pleurisy and otitis media, are decidedly more frequent.

*Pneumonia in Old Persons.*—The disease often begins insidiously without a distinct chill. The temperature is rarely high. Pain, cough and expectoration may be very slight or entirely absent and the physical signs uncertain. The chief features are usually the great prostration, which is out of all proportion to the severity of the local symptoms, and the tendency to speedy collapse.

*Pneumonia in Drunkards.*—The pulmonary symptoms are frequently inconspicuous. Fever may be slight. The striking feature is the marked tendency to delirium, either of a muttering or maniacal character. Actual delirium tremens is not uncommon. There is pronounced asthenia and sudden collapse is not unusual.

*Abortive or Ephemeral Pneumonia* (Larval Pneumonia).—These terms are applied to mild forms of pneumococcic infection in which resolution takes place in the course of two or three days. The early symptoms may be well developed, but the local lesion may not advance beyond the stage of engorgement. Of 1,157 cases of pneumonia studied by Steiner,[1] 23 (2 per cent.) ended in recovery on the third day or earlier. Leube, Weil and others have reported cases of one-day pneumonia.

*Central Pneumonia.*—Cases are not infrequently seen in which the subjective symptoms point indubitably to lobar pneumonia, but in which the objective evidence of pneumonic infiltration remains more or less in abeyance for three or four days. In many cases this anomaly is to be attributed to a tardy development of the exudative process; in others, however, it is apparently due to the gradual extension of a small central lesion toward the periphery of the lung.

*Migratory or Wandering Pneumonia.*—In this form the specific inflammation shows a tendency to involve successively one portion of lung after another. Occasionally the final crisis does not occur until the disease has affected the greater part of both lungs.

*Massive Pneumonia.*—This is a comparatively rare form of pneumonia in which the fibrinous exudate, instead of being confined to the alveoli, extends into the bronchioles and even into the larger bronchi. In such cases the physical signs closely resemble those of pleural effusion.

*Adynamic or Typhoid Pneumonia.*—These terms have been used to designate a type of the disease in which the toxemia is especially marked and the patient rapidly passes into the so-called typhoid state, with a dry, brown tongue, muttering delirium and extreme prostration. In many cases tympanites, diarrhea and slight jaundice are also present. The term typhoid pneumonia as applied to these cases is inaccurate and should be avoided, as the condition has nothing to do with typhoid fever.

*Secondary and Terminal Pneumonias.*—Pneumonia is a common complication of many diseases. When it occurs in the course of another infection, such as typhoid fever, influenza, diphtheria or tuberculosis, it is known as a secondary pneumonia, and when it develops at the close of a chronic disease, such as arteriosclerosis, nephritis or diabetes, it is usually spoken of as a terminal pneumonia. In both forms other microörganisms are frequently present in association with the pneumococcus. The symptoms of the pulmonary infection are often latent and masked by those of the primary disease.

*Postoperative Pneumonia.*—Surgical operations of various kinds, especially those affecting the abdomen or throat, are occasionally followed by pneumonia. Among 57,842 operative cases collected from a number of sources by Anders,[2] pneumonia occurred in 46, or in 0.7 per cent. The advocates of chloroform anesthesia are inclined to speak of this complication as *ether pneumonia*, but it has not been demonstrated that ether is more likely to cause the disease than chloroform. Moreover, statistics show that the disease followed operations as frequently before the days of anesthesia as at the present time, and Mikulicz asserts that the percentage of acute pulmonary complications following major operations is even larger with local than with general anesthetics. It is probable that there is no one cause to which all cases can be assigned. The important etiologic factors appear to be impairment of the patient's resistance by the shock of the operation or by the prolonged anesthesia, exposure of the patient during the operation, aspiration

[1] Deutsch Archiv. f. klin. Med., Vol. 64.
[2] Univ. Med. Magazine, Aug., 1898.

of the infective secretions from the nasopharynx into the lungs during narcosis, and the lodgment of emboli in the vessels of the lungs.

Postoperative pneumonia is more often lobular than lobar. When lobar it frequently lacks the characteristic features of the ordinary frank type of the disease. As a rule, the invasion is marked only by an accession of fever and slight thoracic pain. The mortality ranges between 35 and 50 per cent.

**Complications.**—The complications of lobar pneumonia, for the most part, are excited by the pneumococcus; in some cases, however, they are the result of an associated or intercurrent infection.

*Pleurisy* is the most frequent of the complications. The pleura over the affected lobe is almost invariably involved, but as a rule the inflammation is so mild that it escapes recognition, or is manifested only by a slight stitch in the side and a to-and-fro friction sound. In many cases, however, the pleurisy is well-marked and productive of a more or less copious effusion, the infection assuming the form of a veritable *pleuro-pneumonia*. Pleurisy with definite signs of effusion occurs in about 6 to 8 per cent. of all cases of ordinary lobar pneumonia. In about one half of the cases the effusion is purulent. In children pneumonia is much more likely to be followed by empyema than in adults. Morse[1] observed empyema in 8 per cent. of 118 cases of lobar pneumonia in infancy and Gossage[2] in 12 per cent. of 759 cases.

*Pericarditis* is less common than pleurisy. The exudation may be serofibrinous, fibrinous, or purulent. Chatard[3] found it present in 31 (4.66 per cent.) of 665 cases of pneumonia in the Johns Hopkins Hospital. The pneumonia affected both lungs in 13 cases, the right side only in 13 cases, and the left side only in 5. Pleurisy was present in 28 of the cases. The mortality in the 31 cases was 93.5 per cent. Berry [4] found the pericardium affected in one-third of 400 cases of pneumonia at necropsy.

*Endocarditis*, both simple and ulcerative, not rarely occurs, but with what frequency it is difficult to estimate. It was met with in 45 (10.5 per cent.) of 528 fatal cases of pneumonia. Pye-Smith observed ulcerative endocarditis 7 times in 425 cases of pneumonia. The lesions, which resemble those produced by Streptococcus hæmolyticus, are usually in the left side of the heart, and in a large proportion of the cases meningitis is also present, both infections being of hematogenous origin.

*Meningitis* is an extremely fatal but comparatively rare complication. The frequency of its occurrence varies in different outbreaks. It was noted in 64 of 16,333 cases of pneumonia analyzed by Preble.[5] Autopsy records, of course, show a much larger percentage. Holt[6] observed it four times in 500 cases in children. Proved pneumococcus meningitis is almost invariably fatal.

*Middle ear disease*, usually suppurative, is not an uncommon complication, especially in children, in whom it may produce symptoms simulating meningitis. It was present in 18 per cent. of the 118 cases of lobar pneumonia in infants studied by Morse.

*Arthritis* is an interesting complication, of which Bulkeley[7] in 1914 was able to collect 172 records. It usually develops during or shortly after the pneumonia, but may precede the latter by several days, and occasionally it occurs independently of any pulmonary localization, invasion taking place

[1] Archives of Pediatrics, Sept., 1914.
[2] Proc. Royal Soc. Med., 1907–8, i.
[3] Johns Hopkins Hosp. Bull., Oct., 1905.
[4] Med. Clin. North America, Sept., 1920.
[5] Chicago Med. Recorder, Sept., 1899.
[6] Arch. of Ped., 1893, vol. x.
[7] Ann. of Surg., Jan., 1914.

through a wound or a suppurating middle ear. The lesions are monarticular in about three-fourths of the cases, and show a predilection for the large joints, especially the knee-joint. Other complications are frequently present and suppuration is the rule. Of fifty-two cases tabulated by Herrick,[1] 34 proved fatal.

*Thrombophlebitis* was observed in 10 of the 949 cases of pneumonia cited by Sears and Larrabee. It usually occurs as a sequel, rather than as a complication, and in the vast majority of cases affects the veins of the lower extremities. Occasionally, however, the cerebral sinuses are involved as in 2 cases cited by McCrae[2] and in 1 reported by Ogle.[3]

*Arterial embolism* from the detachment of a cardiac thrombus is extremely rare.

*Nephritis.*—Well developed nephritis is an infrequent complication, although cloudy swelling of the kidney, of varying intensity, probably occurs in all cases.

*Parotitis*, usually suppurative, is occasionally met with. According to Jurgensen it occurs in 0.1 per cent. of all cases. In 1910 Zesas[4] collected from the literature 27 cases.

*Acute dilatation of the stomach* is a somewhat rare complication, but a very dangerous one unless promptly treated. In 1911 Fussell[5] reported 5 cases and collected 6 others from the literature.

*Peritonitis* as a direct sequel of croupous pneumonia is very rare. Fawcett[6] found evidence of it in only 5 of the 182 fatal cases of pneumonia which were at Guy's Hospital in five years.

*Pseudomembranous inflammation of the mucous membranes* especially of the mouth, throat or colon, is occasionally observed. In a case reported by Cary and Lyon[7] nearly all the mucous surfaces of the body were involved.

*Peripheral neuritis* after pneumonia is very unusual. Biermann[8] has reported three cases and collected 6 others from the literature. The brachial plexus is the usual site.

*Hemiplegia* has occasionally been observed. In some instances it has been the result of localized meningoencephalitis. Cases of *suppurative choroiditis*, probably of embolic origin, have been reported by Arlt, Piechaud, Peters and others.

*Acute encephalitis* and *acute myelitis* of pneumococcic origin are rare complications.

*Delayed resolution* is not very uncommon, especially if we include under this head all the cases in which the signs of consolidation persist longer than two or three weeks. Sello[9] observed it in 2.1 per cent. of 750 cases of pneumonia and McCrae in 1.9 per cent. of 486 cases. It is somewhat more frequent in old and debilitated individuals than in young and robust subjects, but there is nothing in the course of an attack of pneumonia by which this peculiar termination can be predicted. The essential feature is the persistence of the physical signs of consolidation—dulness on percussion, exaggerated fremitus, bronchial breathing, and perhaps rales—for several weeks after the occurrence of defervescence. Expectoration is often absent.

[1] Amer. Jour. Med. Sci., July, 1902.
[2] Amer. Med., Jan. 23, 1904.
[3] Trans. Path. Soc. of Lond., Vol. VI.
[4] Fortschr. d. Med., 1910, 27, No. 34.
[5] Amer. Jour. Med. Sci., Dec., 1911.
[6] Lancet, Jan. 16, 1904.
[7] Amer. Jour. Med. Sci., Sept., 1901.
[8] Deutsch. med. Woch., 1913, xxxix, No. 4.
[9] Zeit. f. k. Med., xxxvi, 1899.

In some cases there is only a partial defervescence, slight, irregular fever continuing throughout the entire period of consolidation. Empyema and abscess of the lung should always be considered in the diagnosis. In the majority of cases, after the lapse of three or four weeks, or even a much longer period, absorption takes place and the lung is ultimately restored to its normal condition. Less frequently death results from exhaustion. This termination was noted in 5 of the 16 cases cited by Sello. Occasionally, the fibrinous exudate in the alveoli gradually undergoes fibroid change, with the production of chronic interstitial pneumonia, a condition which is incurable, but essentially chronic.

*Abscess* and *gangrene of the lung* are unusual terminations of true croupous pneumonia. The former probably occurs in about 1 per cent. of all cases, and the latter is even less frequent. Sometimes the two conditions coexist.

*Relapse and Recurrence.*—Actual *relapse* in pneumonia, that is a return of all the characteristic local and general phenomena of the disease several days after complete defervescence and the restoration of the lung to its normal condition, is extremely rare. Cases have been reported by Wagner, Ruge, Ebstein, Osler, Oliver and others, but the whole number on record probably does not exceed a score. The relapse, which is rarely so severe as the original attack, usually occurs after an afebrile period of from 4 to 15 days. On the other hand, *recurrence* of pneumonia in the same individual after an interval of one or more years is common, a history of previous attacks being obtainable in from 10 to 15 per cent. of all cases. Patients do not often have more than three or four attacks, although there are some notable exceptions to this rule.

**Diagnosis.**—Typical cases of lobar pneumonia are recognized without difficulty. It is in the atypical forms of the infection, such as occur in children, in the aged, and in persons suffering from other diseases, that errors in diagnosis are likely to arise. In children, pneumonia may closely simulate meningitis, pleurisy or acute abdominal disease. From *meningitis* pneumonia may be distinguished by the evidence afforded by careful physical examination of the chest and study of the fluid obtained by lumbar puncture. Hurried breathing and an expiratory moan or grunt suggest pneumonia, while an infrequent pulse, Kernig's sign, strabismus and paralysis of individual cranial nerves indicate meningitis. In children the physical signs of *pleuritic effusion* may exactly mimic those of pneumonic consolidation and it may require an exploratory puncture to clear up the diagnosis. When the pain of pneumonia is referred to the course of the abdominal nerves the resemblance to intra-abdominal conditions, especially *appendicitis* and *cholecystitis*, may be close. In pneumonia, however, definite physical signs of disease may usually be elicited over the lungs, the respirations are hurried, the abdominal resistance at the site of the pain generally relaxes during inspiration, and both abdominal pain and tenderness often subside when the patient holds his breath (Rathbun).

In the aged and in persons suffering from cardiovascular disease, nephritis, diabetes, or other chronic disorders, every unusual indisposition, no matter how slight, especially if accompanied by a rise of temperature and an acceleration of the pulse should excite a suspicion of pneumonia and lead to a thorough examination of the chest, otherwise many latent forms of the disease will fail of recognition.

In differentiating between so-called typhoid pneumonia and *typhoid fever with pneumonia* the history of the case should be carefully considered. When pneumonia complicates typhoid fever it usually appears late, and is

preceded by the usual symptoms of the primary disease. The roseolar rash and the Widal reaction are also valuable aids in the diagnosis.

*Acute pneumonic tuberculosis* closely resembles lobar pneumonia in mode of onset, symptoms and physical signs, and sometimes it is impossible to distinguish between the two conditions until 2 or 3 weeks have elapsed. A knowledge of pre-existing tuberculosis or a history suggestive of tuberculosis, involvement of the upper lobes and long duration of the illness should lead one to suspect tuberculous pneumonia. A history of previous good health, involvement of the lower lobes, and the presence of herpes are strongly in favor of lobar pneumonia, as is also a high leucocyte count, although the latter may be observed also in pneumonic tuberculosis. The presence of pneumococci in the blood is, of course, proof of pneumonia, but a negative culture is without significance. Usually at the end of two weeks in acute tuberculosis the temperature assumes a hectic type, profuse perspiration occurs and the patient expectorates large quantities of purulent sputum in which tubercle bacilli can readily be demonstrated. Somewhat later, signs of excavation appear.

The differential diagnosis between *edema of the lung* and pneumonia is rarely attended with difficulty. In edema there is absence of chill, fever and pain, and the râles are not limited to one lobe or one lung.

The differentiation of *bronchopneumonia* from lobar pneumonia is considered on page 590 and that of *pleurisy* in adults from lobar pneumonia on page 620.

**Prognosis.**—The mortality of lobar pneumonia varies somewhat in different localities. Even in the same locality the disease is more dangerous at one time than another, probably because of differences in the prevailing types of pneumococci. It has been shown that cases due to Type I and Type II are of average severity; that those due to Type III are very severe, about one-half of the patients dying; and that those due to organisms of Group IV are mild. However, it is to individual factors, such as age, habits, and previous health of the patient that the greatest importance is to be attached in determining the prognosis. In large general hospitals, where a great many alcoholic and debilitated patients are treated, the mortality is high—ranging from 20 to 40 per cent. On the other hand in armies and navies, owing to the good physical condition of the men composing these bodies, the death rate in time of peace ranges from 5 to 15 per cent. In private practice the mortality varies from 15 to 20 per cent. according to the character of the cases of each individual observer.

The prognosis is greatly influenced by age. In infancy the death-rate is much higher than in childhood, in which period it is from 3 to 10 per cent. After 60 the prognosis is very grave, and after 70 few recover. Sex has no influence on the prognosis. The mortality is somewhat greater in negroes than in whites. In drunkards pneumonia is extremely fatal. The more feeble the patient at the time of the attack the less is the likelihood of his recovery. In vigorous young adults the outlook is usually good, but in persons with diabetes, chronic nephritis, advanced arteriosclerosis, heart-disease, or emphysema, the prognosis is unfavorable. Pregnancy, especially when advanced, is a source of danger to both mother and child. Fat subjects bear pneumonia badly.

In addition to these factors there are certain features of the disease itself which influence the prognosis. Bilateral pneumonia is somewhat more dangerous than the unilateral form. The extent of the lung tissue affected however, does not have much bearing on the prognosis. Statistics do not support the prevailing view that apical pneumonia is more fatal than basic.

Pronounced toxemia, indicated by a pulse-rate persistently above 120, a progressive fall in the peripheral blood-pressure, severe nervous symptoms, abdominal distention and exhaustion, is always of serious import. The occurrence of pulmonary edema in the unaffected parts of the lung is also of ill omen. The absence of leucocytosis, except in cases that are obviously very mild, is distinctly unfavorable, although, as Cabot remarks, the presence of leucocytosis is no guaranty whatever of a favorable issue. A high temperature is not in itself necessarily serious. A high grade of blood infection as shown by the number of colonies per cubic centimeter in the blood plates makes the outlook very unpromising (Cole) and this is true also of the localization of the infection in other parts of the body. Meningitis is almost surely fatal.

**Prophylaxis.**—As it has been shown that pneumonia is acquired chiefly by infection from without, its prevention calls for the same general measures that have been found useful in controlling the spread of other contagious diseases. Isolation of the patient should be practiced, if possible. It is especially important in camps, barracks, hospitals, etc. The sputum and all articles that have been in close contact with the patient should be sterilized.

Persons suffering from acute infections of the respiratory tract, such as coryza and bronchitis, etc., should be cautioned against fatigue and chilling. Nurses and others in attendance upon pneumonia patients should take every precaution against transmitting the disease to others. For ridding the mouth of virulent pneumococci in convalescents and persons who have been in intimate contact with cases of pneumonia Kolmer recommends ethylhydrocuprein hydrochlorid or quinin bisulphate, 1 : 10,000 dilution in some weak antiseptic solution, as a mouth wash, gargle and nasal douche.

Preventive inoculation by vaccines holds out much promise. At Camp Wheeler Cecil and Vaughan[1] found that the incidence rate of pneumonia of all types among vaccinated troops (13,460) was less than one-half that among the unvaccinated. A single inoculation consisting of 1 mil of an oil suspension containing 10 billion each of pneumococci of types I, II, and III was sufficient. Lister[2] found that the immunity lasted at least 9 months.

**Treatment.**—*Absolute rest* is imperative and should be enjoined even if there is only a suspicion that pneumonia is developing. The bed pan should be used throughout the attack, and moving the patient for bathing and physical examination should be avoided so far as possible. The number of visitors to the sick-room should be strictly limited. In cases of average severity, without complications, the patient may be allowed to sit up after the temperature has been normal for a week or ten days.

An abundance of *cool fresh air* is essential. The windows of the sick-room should be kept wide open, regardless of atmospheric conditions. Except in the case of very young children, old persons and frail patients treatment out-of-doors on an open porch or balcony is usually advisable. Screening from drafts, however, is necessary, and in cool weather the patient must be well protected by blankets and suitable underclothing to prevent chilling. Under no circumstances should his body be exposed for bathing or examination in the open air. That the nurse in charge of the patient should be warmly clad is equally important. If the outdoor treatment makes the patient more uncomfortable and more restless, it should not be enforced.

The *food* should be nourishing but easily digestible. Milk, junket, broths, soft boiled eggs, strained oatmeal gruel, custards, blanc mange and calf's-foot

[1] Jour. Exp. Med., 1919, xxix, 457.
[2] South African Institute for Med. Research, 10: 1917.

jelly are suitable forms of nourishment. Cool water should be given freely between meals. The bowels should be moved regularly, using for the purpose, if necessary, mild laxatives or enemas.

Even if the temperature is not high, *hydrotherapy*, especially cold sponging, is of service, provided it can be carried out without causing much disturbance of the patient. The use of tub-baths or packs is inadvisable. Except for the purpose of combating certain symptoms, *local applications* are useless. If there are no special indications the chest may be enveloped in a light padded jacket.

**Specific Treatment.**—Workers in the Rockefeller Institute have demonstrated that in pneumonia due to pneumococcus of Type I, which is responsible for about one-third of all cases, homologous immune horse-serum is highly effective, especially if used early in the disease, reducing the mortality to about 7 per cent. Homologous serums in pneumonia due to other types of pneumococci are much less efficacious and polyvalent serums are of doubtful value. The usual dose of serum is 90 to 100 mils, preferably diluted with salt solution, intravenously, every eight hours until a definite effect has been obtained. The danger of an anaphylactic shock may be reduced to a minimum by injecting subcutaneously 0.1 to 1 mil of horse serum an hour before the serum treatment and by administering the serum very slowly, especially at first (15 minutes for the first 15 mils).

Stengel[1] reports very encouraging results from intravenous injections (30 mils) of blood-serum obtained from pneumonia patients just following the crisis. Favorable results have also been reported from intravenous injections of non-specific proteins, but this treatment produces severe reactions.

**Symptomatic Treatment.** *Pleuritic Pain.*—In many cases this may be relieved by the application of a mustard plaster, turpentine stupe or ice-bag. The use of a few wet or dry cups is still more effective. If the pain is very severe, morphin should be given hypodermically.

*Cough.*—Frequent and unproductive cough is best controlled by codein in doses of $\frac{1}{8}$ to $\frac{1}{6}$ gr. (0.008–0.01 gm.) by the mouth. Expectorants are not usually needed. If, however, there is much bronchial catarrh and the expectoration is very viscid ammonium chlorid or potassium citrate may be of service.

*Circulatory Failure.*—The use of circulatory stimulants as a routine measure is probably better avoided. Cole and other workers in the Rockefeller Institute, however, recommend the administration of digipuratum (8 gr.–0.5 gm. a day by the mouth), or a corresponding dose of some other preparation of digitalis, for a period of two days. The purpose of this early administration of the drug is not to produce immediate effects upon the heart, but to put the patient into such a condition that later if need arises physiologic digitalis effects may quickly be obtained by the administration of small doses by the mouth. Whether digitalis is used from the beginning or not, it is indicated when the pulse becomes unusually accelerated and weak. If it fails caffein or strychnin may be used as an adjuvant or as a substitute. These two drugs are useful also in combating respiratory depression, which is sometimes responsible for circulatory failure. Alcohol, as a rule, is better avoided unless there is an alcoholic history, and even then it should be used only in moderate amounts, that is to the extent of about 3 or 4 ounces (90–120 mils) in the twenty-four hours. Atropin is often of value when there is excessive bronchial secretion or a tendency to pulmonary edema.

In acute heart failure an intravenous injection of strophanthin ($\frac{1}{80}$ gr.–0.00075 gm.) is sometimes very effective, but under no circumstances

[1] Med. Clin. of North Amer., Jan., 1921.

should this treatment be employed if the patient has been taking digitalis. If strophanthin cannot be given, camphor (2 gr.—0.13 gm.—in sterile olive oil every two hours) or adrenalin (15 to 30 min.—1 to 2 mils—in saline solution and very slowly administered) should be tried. In cases with embarrassment of the right ventricle, as shown by marked cyanosis and extension of the area of heart dulness toward the right, moderate venesection is indicated. Oxygen makes the breathing somewhat easier and to this extent aids in conserving energy.

*Insomnia.*—In the early stages of the disease, morphin is beneficial and safe. Later, preference should be given, as a rule, to bromids, chloral or veronal.

*Abdominal Distention.*—In the milder cases the application of turpentine stupes and the use of asafetida enemas usually suffice. Hot saline solution by proctoclysis is sometimes useful. The introduction of a rectal tube may also prove effective. In severe cases pituitary extract (15 min.–1 mil., subcutaneously, every two hours) or physostigmin salicylate ($\frac{1}{60}$ gr.–0.001 gm. subcutaneously, and repeated in three hours) may afford temporary relief.

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## MENINGOCOCCUS INFECTION

Infection with the meningococcus, as a rule, gives rise to inflammation of the investing membranes of the brain and spinal cord, and, therefore, it has been commonly referred to as cerebrospinal fever or epidemic cerebrospinal meningitis. Occasionally, however, the meningococcus, despite its strong affinity for the meninges, produces a general septicemia without any special localizations or with a localization in some particular structure other than the meninges, such as the joints, the pleura, the accessory nasal sinuses, or the endocardium. In 5 per cent. of 350 cases of meningococcus infection studied by Herrick[1] meningitis did not develop. The cases of meningococcus endocarditis studied by Cecil and Soper[2] were of the acute vegetative variety and similar to those caused by Streptococcus hæmolyticus or pneumococcus.

### CEREBROSPINAL FEVER

(Epidemic Cerebrospinal Meningitis)

**Definition.**—Cerebrospinal fever is a specific, infectious disease, caused by Diplococcus intracellularis meningitidis, occurring in epidemics or sporadically, and characterized anatomically by inflammation of the cerebral and spinal meninges and clinically by an irregular febrile temperature, divers nervous symptoms, and not rarely a petechial or purpuric eruption.

**History.**—The disease was first recognized as a distinct affection by Vieusseux, who described the outbreak in Geneva in 1805. In the following year Danielson and Mann drew attention to its prevalence in Medfield, Massachusetts. Since that time it has appeared in nearly every civilized country, and frequently in places widely separated from each other. The epidemic occurrence of the disease has been grouped by Hirsch into four periods. In the first period (1805–1830) America was seriously involved, only isolated outbreaks occurring in Europe. During the second period

[1] Archiv. Int. Med., April 15, 1919.
[2] Archives of Internal Medicine, July, 1911.

(1837–1850) widespread epidemics occurred in France, Algiers, Italy, Denmark, and America. In the third period (1855–1875) the disease prevailed extensively in Europe, especially in Germany, and visited a number of localities in America. In the fourth period (1875 to the present time) the infection has been widely diffused, epidemics of a varying magnitude occurring in a great number of places. In the years 1904 and 1905 there were more than 2000 deaths from cerebrospinal fever in New York City.

Owing to the frequent occurrence of a hemorrhagic eruption in many of the early New England outbreaks, the disease became known as "spotted fever," but this name is now obsolete.

**Etiology.**—The organism known as Diplococcus intracellularis meningitidis, or simply as the meningococcus, which was isolated first by Weichselbaum in 1887, is the essential cause of the disease. Morphologically, this bacterium resembles the gonococcus and pneumococcus. It occurs in biscuit-shaped pairs or tetrads; it stains with the usual anilin dyes, but is decolorized by Gram's method; it is non-motile and produces no spores; it is sensitive to cold and to desiccation, and is not easily kept alive on culture media. Blood-agar is best adapted to its growth. It is now definitely known that with meningococci, as with pneumococci, there is not a single, uniform kind of microörganism, but a group containing several types, clearly distinguishable by specific agglutination tests, and some more pathogenic than others. According to Flexner, two types of the entire group are responsible for from 75 to 80 per cent. of all cases of epidemic meningitis. In the course of the disease, the meningococcus may usually be found in the spinal fluid and in the secretions of the nose, throat and conjunctiva, and in some cases, especially early in the attack, it may be isolated from the blood. In the inflammatory exudate the organism occurs chiefly within the bodies of the polymorphonuclear leucocytes.

Under ordinary conditions a relatively high percentage of normal persons in a community harbor the less pathogenic varieties of the meningococcus in their mouths, and when cerebrospinal fever is present a greater or less number of healthy carriers of the dangerous types of the organism may always be found.

The disease is communicable from person to person, although its contagiousness is of a comparatively low order, individual susceptibility being a very important factor. Physicians, nurses or other attendants upon the sick are only rarely attacked. Recent studies have shown that the nasopharynx is the chief point both of entrance and exit of the virus, and that the latter is disseminated principally, if not entirely, through the agency of minute droplets of secretion that are expelled in coughing, sneezing, etc. The healthy carrier who has picked up pathogenic meningococci from others is undoubtedly a much greater menace than the meningitic patient himself. In every epidemic the carriers outnumber many times the cases of disease. The duration of the carrier state is usually from 2 to 4 weeks, but it may be very much longer.

It has generally been surmised that the meningococci gain access to the meninges directly through the ethmoid or sphenoid sinuses, but recently many cases have been reported in which the organisms have been found in the blood before the occurrence of the meningitic symptoms and while the spinal fluid was still clear and sterile, and therefore it is probable that in some instances, at least, the meningococci first enter the general circulation from the nasopharyngeal mucous membrane, producing a general septicemia, and then by a process of metastasis become localized in the meninges, for which they have a special affinity.

Overcrowding and inadequate ventilation are important subsidiary factors in the spread of the disease; hence epidemics begin, as a rule, in cold weather, and the first cases are usually in the houses of the poorer classes. In some outbreaks, however, the large cities have been completely spared, while small villages, widely separated from one another, have suffered severely. Once the infection has become thoroughly established in a community it claims its victims from among the rich and poor alike. Although cerebrospinal fever often prevails simultaneously in different parts of the world, it never becomes actually pandemic; indeed, the majority of its outbreaks are confined to a small area of a country, to a single city, or even to a certain part of a city. Epidemics rarely last longer than six months in one locality, but in their wake sporadic cases continue to occur and under favorable conditions these may so increase in number as to form another epidemic.

Although in some outbreaks the majority of cases have been in adults, the disease is usually much more prevalent among children and adolescents. Of 2179 cases occurring in New York in 1904 and 1905, 67 per cent. were in persons under 10 years of age and 15 per cent. were under 1 year (Billings). In the Silesian outbreak, 90 per cent. of 3,102 patients were under 15 years of age (Westenhoeffer). Cerebrospinal fever is rare after 50. Sex is apparently without influence. Excessive fatigue, insufficient food, exposure to inclement weather, etc., increase individual susceptibility. Military life, with its unusual conditions, involves a special liability to the disease, fresh recruits in camps often suffering severely. In 1898 Councilman, Mallory and Wright[1] were able to collect from the literature but 5 cases in which the same individual is reported to have been infected twice, but in outbreaks occurring during the World War recurrences were apparently not very rare.

**Morbid Anatomy.**—In very acute cases the body may be well nourished, but in long-standing cases it is extremely emaciated. Petechiæ and herpes are sometimes found on the skin. The lungs frequently exhibit congestion and evidences of pneumonia, usually of the lobular variety. Ecchymoses may be seen in all the serous membranes, and especially in the pericardium. The spleen is usually enlarged, but rarely to the same extent as in other acute infections. The heart, liver and kidneys present varying degrees of cloudy swelling. Occasionally, there is actual nephritis. The stomach and intestines are not much altered, as a rule, but enlargement of Peyer's patches and of the mesenteric lymph-nodes has been noted in some outbreaks.

The most characteristic changes are found in the central nervous system. There is inflammation of the meninges, accompanied by a sero-purulent or fibrino-purulent exudation, extending some distance into the tissue of the brain and cord and along the nerves. The lesions are usually most marked at the base of the brain and posterior aspect of the cord, but all parts may be affected. In very acute cases of but a few days duration scarcely more may be seen than intense injection of the pia-arachnoid with a little sero-purulent exudation in the sulci along the distended vessels. In cases that have lasted one or two weeks the exudation is more extensive and contains considerable fibrin. In chronic cases the membranes are thickened, opaque and edematous. The substance of the brain and cord not rarely presents scattered punctate hemorrhages and minute foci of necrosis. The ventricles contain an excess of turbid fluid and the choroid plexuses are usually swollen and covered with sero-purulent exudate. Microscopic examination of the tissue shows definite changes, which are nearly always more marked in the brain than in the cord. The walls of the bloodvessels, the perivascular spaces and the

[1] Amer. Jour. Med. Sci. Mar., 1898.

surrounding tissue for some distance inward from the meninges are infiltrated with polymorphonuclear leucocytes, and many of the ganglion cells are granular and fatty.

The cranial and spinal nerves are involved to a greater or less extent in nearly all cases of cerebrospinal meningitis.

**Symptoms.** *Ordinary Form.*—The *period of incubation* is not definitely known, but it is supposed to be from 1 to 4 or 5 days. In some instances the attack is preceded by sore-throat or coryza, but in the majority of cases prodromes are absent and the disease begins suddenly.

The invasion is usually marked by a chill or chilliness, muscular pains, severe headache, repeated attacks of vomiting, and general febrile disturbances. In children there may be convulsions. The vomiting, which is a very constant feature, usually passes off quickly, although it may recur at irregular intervals throughout the illness. Vertigo frequently appears with the headache and may persist even when the patient is recumbent.

In a short time, usually within 24 or 36 hours, the invasion is followed by pain at the nape of the neck, along the spine, and even in the limbs, with hyperesthesia and tonic muscular spasms. In some cases the hyperesthesia is so intense that the patient can scarcely bear the weight of the bed-clothes. The muscular rigidity is usually limited to the postcervical and dorsal regions, but it may be general. Accompanying it there is often retraction of the head and in severe cases orthotonos or opisthotonos. The decubitus is commonly lateral with the thighs flexed upon the abdomen and the legs upon the thighs. In extreme cases, especially in children, the head may be thrust back so far that the occiput rests between the shoulders, or possibly within a few inches of the buttocks. In no other form of meningitis is rigidity of the neck such a conspicuous feature. Muscular twitchings are sometimes observed.

Kernig's sign (inability to extend fully the leg when the thigh is at a right angle with the trunk) is almost always obtainable and is another indication of muscular hypertonicity. While its absence does not exclude meningitis, its presence makes the existence of the disease highly probable. The cutaneous reflexes are usually increased, but the tendon-reflexes vary greatly. Babinski's toe reflex is occasionally present. Paralyses sometimes develop in the course of the disease, but excepting those affecting the extraocular muscles (strabismus), they are somewhat uncommon.

The special sense organs are almost always involved. Photophobia may be present at the onset. Conjunctivitis is often noted. The pupils are variable; frequently they are dilated and unequal. Strabismus is common, and nystagmus, conjugate deviation, and ptosis may occur. Retraction of the lids is not very rare, and is probably the result of hydrocephalus. Optic neuritis may occur, but it is less common than in tuberculous meningitis. A striking feature in many cases is the marked variation in the eye symptoms from day to day. Otitis media is not an infrequent complication. Deafness from involvement of the eighth nerve is fairly common and may be permanent. Tinnitus aurium is sometimes an early symptom. The mental condition is variable. As a rule, there is drowsiness or actual stupor, which may be interrupted by delirium. Occasionally the latter becomes maniacal. In mild cases the mind may be clear or even abnormally acute until recovery.

The face is more often pale than flushed. At times it may present a cyanotic hue. Herpes, chiefly about the lips and nostrils, but occasionally covering large areas of the face and neck, is found in from 20 to 40 per cent. of the cases. A petechial or purpuric eruption is common in some epidemics, while in others it is observed only exceptionally. It bears little or no relation to the severity of the attack and may appear at any period of the disease.

Recently cases have been observed in which the eruption preceded the meningitic symptoms by several days, the condition at first being apparently one of ordinary infectious purpura.

Urticarial, roseolar, morbilliform and pemphigoid eruptions likewise occur in some cases. Trousseau's tâches cérébrales (persistent red lines after stroking the skin) may usually be elicited, but they are by no means pathognomonic.

The temperature is irregular and presents no distinctive curve. As a rule it ranges between 101° and 104° F., but just before death it may rise abruptly to 106° or even 107° F. In some of the most severe cases it never exceeds 101° and rarely it is normal throughout the greater part of the disease. The pulse-rate is usually accelerated (100-120), but it may be abnormally low (60-50). Irregularities both in rhythm and force are frequently observed. The respiration, too, is generally quickened, sometimes out of proportion to the pulse and temperature. As the disease advances it not rarely acquires the Biot or the Cheyne-Stokes rhythm. The tongue is coated and in serious cases it may become dry and brown. Constipation is the rule. The spleen may or may not be enlarged. Traces of albumin and a few casts are not rarely found in the urine. Retention of urine is not uncommon. A polymorphonuclear leucocytosis is present in the great majority of cases and usually develops at an early period. The count is, as a rule, above 20,000 and may be above 40,000. Emaciation is a striking feature in long standing cases.

Cytologic and bacteriologic examinations of the fluid obtained by lumbar puncture afford a valuable means of determining not only the existence of meningitis, but also the exact character of the infection. The findings vary somewhat with the stage of the disease. In the first twenty-four hours the fluid may be clear, sterile and only slightly increased in amount. Later and for a considerable period it is characteristically changed. It is turbid or even purulent, is under increased pressure, shows an increase in albumin and globulin, is rich in cells, most of which are polymorphonuclear leucocytes, and contains the specific organisms. In long-standing cases the fluid again becomes clear, at least in the intervals between exacerbations, and usually shows an excess of lymphocytes.

*Fulminating Type.*—This type, which is comparable to the malignant forms of other specific infections, is not uncommon in some outbreaks and occasionally appears sporadically. The patient is suddenly stricken, sometimes without the least warning, and quickly passes into a state of collapse. A severe chill, headache, stupor, sometimes interrupted by delirium and soon followed by coma, spasmodic contractions of the muscles, moderate fever, a feeble pulse, and extreme prostration are the usual symptoms in such attacks. A purpuric eruption is also present in some cases and occasionally hemorrhages occur from the mucous membranes. Death is inevitable and may take place within twenty-four or even within twelve hours. Autopsy reveals hyperemia and opacity of the membranes, but usually no pus.

*Abortive Type.*—In this variety the invasion is more or less severe, but in three or four days all the symptoms subside and the patient enters upon a rapid convalescence.

*Intermittent Type.*—Cases are not rarely met with in which the fever and other symptoms are subject to marked remissions and exacerbations. The temperature curve may bear some resemblance to that of intermittent malarial fever, although it seldom shows the regular periodicity of the latter.

*Chronic Type.*—In nearly every epidemic cases occur in which the attack begins as in the ordinary form, but the course of the disease is protracted over two, three or four months. Such cases are marked by irregular paroxysms of

fever, alternate remissions and aggravations of the nervous symptoms, and extreme emaciation, the patient in many instances being reduced to a mere skeleton. The persistence of the symptoms is to be ascribed, as a rule, to the development of hydrocephalus. Lumbar puncture is frequently unsuccessful owing to obstruction of the ventricular outlet by inflammatory exudate. Death, usually from the increased intraventricular pressure rather than from the infection, is the rule. If recovery ensues it is seldom complete, permanent mental or nervous sequelæ almost always remaining.

The condition known as *posterior basic meningitis*, and which was described by Gee and Barlow in 1878 and again by Still in 1898, is probably one of the forms of chronic cerebrospinal fever occurring in children below the age of two years. The chief features of the disease are marked retraction of the head, muscular rigidity, mental dulness or actual stupor, moderate leucocytosis and extreme emaciation. Blindness is not uncommon. The condition is essentially chronic, lasting from several weeks to many months.

**Complications.**—*Pneumonia*, usually lobular and due in many cases to the meningococcus, is somewhat common. *Pleurisy* or *pericarditis* may accompany the pneumonia or occur independently of it. A few cases of *acute vegetative* (malignant) *endocarditis* of meningococcus origin have been reported.

*Severe conjunctivitis*, *keratitis*, with ulceration of the cornea, and *iridochoroiditis* may occur. *Optic neuritis* is also seen, but it is less common than in tuberculous meningitis. These ocular lesions may be due, according to Councilman, Mallory and Wright, to involvement of the nerves of the eye in the exudate at the base of the brain, to direct extension of the inflammation along the pia-arachnoid of the optic nerve, or to loss of sensation from inflammation of the fifth nerve and destruction of the Gasserian ganglion.

Affections of the *ear* are even more frequent than those of the eye, otitis media being especially common in some epidemics. Inflammation of the eighth nerve may also supervene and lead to permanent deafness or in infants to deaf-mutism.

*Chronic hydrocephalus* from closure of the foramen of Magendie and the foramina of Luschka by inflammatory exudate is a serious and not infrequent sequel. Its development is indicated by persistent headache, vomiting, stupor, impairment of vision, convulsions and other evidences of increasing intraventricular pressure. Macewen's sign (a hollow note on percussion over the inferior frontal or parietal bone when the patient is in an upright position with the head slightly inclined to one side) is also present in many cases. Other sequels probably depending, as a rule, upon hydrocephalus are *mental impairment*, *epilepsy*, *blindness* from optic atrophy, *paralysis of the motor cranial nerves*, and *contractures* and *spastic paralyses* of the extremities.

*Arthritis*, affecting one or several joints and sometimes purulent, is a fairly common complication. Rolleston[1] found it in 4.8 of 502 cases, Herrick and Parkhurst[2] in 6.5 per cent. of 902 cases and Netter and Durand[3] in 5.5 per cent of 200 cases. *Epididymitis* may occur in association with arthritis or as an independent complication.

**Diagnosis.**—*Certain other acute infections*, notably typhoid fever, influenza, and pneumonia, occasionally simulate cerebrospinal fever very closely, lthe resemblance being in the severe headache, vomiting, fever, somnoence, and stiffness of the neck (meningism), but, as a rule, a careful review of all the symptoms, together with the results of a blood-examination and lumbar

[1] Lancet, April 19, 1919.
[2] Amer. Jour. Med. Sci., Oct., 1919.
[3] Bull. de l'Acad. de Méd., 1915, lxxx.

puncture, will make the diagnosis clear. As there is some evidence tending to show that the withdrawal of cerebrospinal fluid during acute general infections may favor the occurrence of meningitis, it is recommended that only small-bore needles be used in making lumbar punctures for diagnostic purposes and that only minimal quantities of fluid be withdrawn (Wegeforth and Latham).[1] It should be borne in mind that meningococci are sometimes present even in fluid that is limpid.

The differentiation of cerebrospinal meningitis, especially the sporadic form, from other varieties of meningitis is sometimes impossible without recourse to lumbar puncture. In *tuberculous meningitis* the onset is usually insidious; a focus of tuberculosis is frequently to be found elsewhere in the body; herpes is rare; retraction of the head is less marked and opisthotonos is uncommon; and the fluid from lumbar puncture is clear, usually shows an excess of mononuclear cells, and often contains tubercle bacilli. *Pneumococcus meningitis* is of decidedly greater gravity than the meningococcus form, and, in general, pursues a more rapid and tumultuous course, but when it occurs independently of pneumonia, the diagnosis can be made with certainty only by finding pneumococci in the cephalorhachidian fluid. The recognition of *streptococcus meningitis* is often aided by the presence of a primary focus of suppuration in the middle ear or in some other part, but here again lumbar puncture will usually make the diagnosis positive.

The meningitic form of *acute poliomyelitis* has symptoms very similar to those of cerebrospinal fever. In poliomyelitis, however, the fluid from lumbar puncture is clear or with a preponderance of small mononuclear cells; paralysis appears early, usually on the second or third day, and leucocytosis is much less constant than in epidemic menigitis. *Epidemic encephalitis* may sometimes cause confusion, but in this disease usually milder disturbances of consciousness (lethargy or somnolence) prevail, rigidity of the neck is slight or altogether absent, ophthalmoplegia is a conspicuous and early feature, and the cerebrospinal fluid is clear, sterile, and moderately rich in small mononuclear cells.

**Prognosis, Course and Duration.**—The outlook is always serious, the mortality varying in different epidemics from 50 to 80 per cent. The disease is especially fatal in early life. More cases end fatally at the beginning of an epidemic than later. Convalescence is usually slow and relapse is not uncommon. Occasionally recrudescence or actual recurrence is observed after a symptom-free interval of two, three, or even four months. Even when recovery occurs serious sequels often persist. The course varies greatly, being completed in some cases within 24 or 36 hours, and in others only after the lapse of several months. The majority of deaths occur within the first week. In individual cases a sudden and violent onset, high temperature, repeated convulsions and early coma are unfavorable features.

**Prophylaxis.**—As cerebrospinal fever is a communicable disease, the same precautions against its spread should be observed as in the case of other serious contagious processes. Carriers being the chief source of infection should be sought for among persons who have been closely associated with cases of meningitis, and when found should be isolated and appropriately treated. Applications of antiseptic chemicals to the nasopharynx by douching and spraying have been employed with considerable success. Gordon and Flack found a 1 per cent. aqueous solution of chloramin of service and Dunham and Dakin[2] recommend a solution of dichloramin-T in oil. Whatever the application, it should be made thoroughly several times a day.

[1] Amer. Jour Med. Sci., Aug., 1919.
[2] Brit. Med. Jour., 1917, i, 682.

Active immunization by the subcutaneous injection of a polyvalent vaccine and passive immunization by subcutaneous injection of antimeningococcus serum have been practiced to some extent, but there are no available statistics to show how effective these procedures are in protecting from infection persons who have been exposed to the disease.

**Treatment.**—The sick room should be quiet, darkened, and well-ventilated. The diet should be light but supporting. Occasionally, in order to secure the ingestion of sufficient nourishment, it may be necessary to feed the patient by means of a stomach tube. The bowels should be opened freely at the onset, preferably by calomel, and then every day or two by a cascara preparation, milk of magnesia, solution of magnesium citrate or a laxative mineral water.

The specific treatment, which consists in the use of a polyvalent antimeningococcus serum, prepared after the method of Jochmann, Flexner and Jobling[1] and others, has apparently reduced the mortality of the disease about one-half. Of 1394 cases treated with serum in the Texas epidemic of 1912 the mortality was 37 per cent., as compared with a mortality of 77 per cent. among 562 cases treated without serum (Sophian[2]). The earlier in the case the serum is used, the better are the results. According to Flexner, of 199 cases treated in the first three days the mortality was only 18.1 per cent. The dose of serum for adults is from 30 to 50 mils, and for infants and children 5 to 20 mils, the amount varying with the quantity of cerebrospinal fluid withdrawn. In children, especially, the dose should be a few mils less than the amount of fluid removed. When only a small amount of cerebrospinal fluid is obtained, not more than 10 mils should be injected. In cases of moderate severity the injections should be given every day for 3 or 4 days and then every other day until the patient's general condition and the result of the examination of the cerebrospinal fluid indicate that the infection has subsided. If the case is severe and not seen until after the third day the first injections should be given every 12 hours. The average case requires in all from 4 to 8 injections. The serum should always be introduced slowly and preferably by the gravity method. If symptoms of collapse appear some of the fluid should be allowed to escape through the needle. Artificial respiration and an injection of atropin sulphate—$\frac{1}{100}$–$\frac{1}{60}$ grain (0.00065–0.001 gm.)—may also be required.

When the patient is seen early and bacteremia can be demonstrated the serum may be given also intravenously, although with this method of administration there are likely to be severe systemic reactions, especially in children. The dose of serum for intravenous injection is from 30 to 120 mils daily for several days, the amount depending upon the age of the patient and the severity of the attack. The injection should always be made very slowly and to avoid serious reactions, it is advisable to desensitize the patient first by giving an hour before the intravenous injection 1 mil of the serum subcutaneously.

Apart from the use of specific serum the treatment is chiefly symptomatic. For headache, restlessness, delirium, insomnia, etc., morphin or codein, preferably hypodermically, is often required. Bromids, sulphonal, etc., are not usually effective. The application of an ice-cap to the head is helpful. Hot baths (105°–110° F.), once or twice a day, for from 5 to 15 minutes, are often of value. If a circulatory stimulant is required, digitalis should be chosen, as strychnin and caffein are likely to increase the nervous excitability. When there are evidences of increased intraventricular pressure and lumbar punc-

[1] Jour. Exper. Med., 1908, x, 141.

[2] Sophian: Epidemic Cerebrospinal Meningitis, St. Louis, 1913.

ture affords no relief, the ventricles may be tapped by trephining or in infants by introducing the needle directly through the anterior fontanel. After tapping, if the fluid is turbid or purulent, a small amount of serum may be injected into the cavity. Stetten and Roberts[1] in an apparently hopeless case successfully drained the ventricle by puncturing the corpus callosum and recommend this procedure in preference to simple ventricular puncture through the cerebral substance. Painful joints may be treated locally as in cases of rheumatism. In refractory arthritis the fluid may be removed from the joint and serum injected.

Rest is essential during convalescence and the return to usual activities should always be effected slowly. Tonics, especially iron, are frequently indicated.

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## TYPHOID FEVER

(Enteric Fever; Abdominal Typhus)

**Definition.**—Typhoid fever is an acute general infection caused by Bacillus typhosus (Eberth-Gaffky), characterized anatomically, in the vast majority of cases, by definite lesions in the lymphoid structures of intestines, in the abdominal lymph nodes and spleen and manifested clinically by continued fever, a roseolous eruption, a specific blood-serum reaction with typhoid bacilli, various abdominal, pulmonary and nervous symptoms and a tendency to certain complications, notably intestinal hemorrhage and perforation.

**History.**—While typhoid fever seems to have been known to Hippocrates and to Galen, definite knowledge of the disease dates from the seventeenth century, when Willis noted many of its essential features and drew attention to the clinical differences between it and typhus fever. Little attention, however, was paid to the writings of Willis, and in the eighteenth century, although Riedel in Germany, Huxham in England, and Bretonneau in France, added greatly to our proper understanding of the affection, the general opinion was that typhoid and typhus fevers were identical. Even Louis, who suggested the name "typhoid fever" and who published the first full and accurate description of the disease, as late as 1829 confused the two conditions. Not until 1837 was it conclusively demonstrated that typhoid and typhus fevers were separate and distinct diseases. The credit of clearly establishing the distinction belongs to Gerhard[2] and Pennock of Philadelphia. The specific organism of typhoid fever was discovered by Eberth in 1880 and isolated by Gaffky in 1884. Widal in 1895 applied the agglutination reactions previously observed by Gruber, Durham, Pfeiffer, and others to the clinical recognition of the disease in its early stages. In 1896 Pfeiffer and Kolle demonstrated that immunity could be produced by the subcutaneous inoculation of dead typhoid bacilli, and a few years later A. E. Wright brought the procedure into clinical application.

**Etiology.**—Typhoid fever is a disease of world-wide prevalence, the incidence in different localities depending largely on the opportunities afforded for the contamination of the drinking water and food by infected human excreta—the primary source of the bacilli. It is endemic in most parts of the United States, and frequently prevails epidemically. Urban or rural life itself does not influence the incidence, and in proportion to population

[1] Jour. Amer. Med. Assoc., Jan. 25, 1919.
[2] Amer. Jour. Med. Sci., Feb. and Aug., 1837.

city and country districts are about equally affected. Outbreaks are especially prone to occur in newly settled localities and in hastily constructed camps where no adequate provision is made for the disposal of excreta and the protection of the water-supply. In the Franco-Prussian war there were 73,396 cases of typhoid fever among the German troops, with a mortality of nearly 12 per cent., and in the Spanish-American war there were 20,738 cases among 107,973 American troops, with a mortality of 19 per cent. In the Anglo-Boer war almost one-third of the entire mortality, including that from wounds, was due to the disease. In the recent European war, owing to improved sanitation and antityphoid vaccination, the incidence of typhoid fever in the American Expeditionary Forces was less than 0.1 per cent.

Typhoid fever is most prevalent in the late summer and autumn months, although it is present to a certain extent throughout the year, and epidemics may occur at any time if there be infection of the drinking water, the milk or other articles of food. The disease occurs at all periods of life, even in infancy and old age, but three-fourths of all cases occur between the fifteenth and thirty-fifth years. Many instances of typhoid infection *in utero* are on record. Being more exposed to infection, the male sex furnishes a larger proportion of cases than the female; sex itself, however, exerts no influence. Proportionately, the poor suffer somewhat more than the rich, the unsanitary conditions and crowding that accompany poverty increasing the chances of direct infection. The state of the individual's health probably has little if any etiologic influence. It has long been known that new-comers in an infected locality are more likely to be attacked than persons who have been resident for some time. One attack usually confers immunity, but recurrences are by no means rare, and an immunity acquired against typhoid fever affords no protection against paratyphoid infections. Certain persons appear to be naturally insusceptible to the disease.

*Bacteriology.*—The exciting cause of typhoid fever is the *Bacillus typhosus*. This organism, like the colon bacillus to which it is closely allied, is rod-shaped, flagellated, and actively motile. It grows readily in ordinary media and develops best in an atmosphere containing oxygen. It does not form spores. It stains with the usual aniline dyes and is Gram negative. Under certain conditions typhoid bacilli may remain alive in water for weeks or months, but under ordinary conditions, owing to the deleterious influence of sunlight, currents, sedimentation, etc., and the antagonism of other bacteria, they probably multiply little if at all in large bodies of water, and when the source of infection is removed tend to die out in a comparatively short time. They may survive for months in the contents of privy vaults and in superficial layers of soil, and may resist drying for days or weeks. Milk is a favorable medium for their growth. They resist freezing and can live in "snow" ice and in ice-cream for at least a month. In solid ice, however, they soon perish. They are killed by a temperature of 60° C. in a few minutes.

As regards the toxins derived from the bacilli we are not fully informed. The most powerful poison is probably an endotoxin liberated when the bacillus undergoes disintegration. A true toxin is also formed by the living organism, but to a limited extent only. Immunity may readily be produced by injections either of living or dead bacilli, but the blood serum of immunized animals and of patients recovering from typhoid fever possesses only feeble antityphoidal properties. Early in the disease specific agglutinins appear in the blood, and their presence is extensively utilized for diagnostic purposes (Widal test).

The bacilli gain entrance to the body by way of the digestive tract, being

introduced with drinking water or food, or accidentally carried to the mouth on soiled fingers. Very rarely, perhaps, the portal of entry may be the respiratory tract. Within the body the bacilli especially develop in the lymphoid tissues of the intestines, in the mesenteric nodes, and in the spleen, but they may also be demonstrated in other organs, in the gall-bladder, in the bone-marrow, in the rose spots on the abdomen, and in the blood. In certain parts of the body they may be present for months or years. The bacilli are eliminated in the feces, in many cases in the urine, and occasionally in the sputum. A small percentage of persons who have suffered from typhoid fever, and rarely persons who apparently have never had the disease, discharge typhoid bacilli intermittently in their excreta for periods of years. The proportion of typhoid patients who become so-called carriers is variously estimated from 2 to 6 per cent. As a rule, the habitat of the bacilli in these cases is the gall-bladder and the avenue of escape the intestines. Occasionally, however, the organisms vegetate in some part of the urinary tract and escape in the urine. Many sporadic outbreaks of typhoid fever in small communities, in asylums, and in households have been traced to carriers, usually women, in some way connected with the handling of food. Sawyer[1] has reported an outbreak consisting of 93 cases, in which the source of infection was a woman who prepared spaghetti served at a public dinner. Soper's[2] investigation of "Typhoid Mary" showed that 26 cases of typhoid fever could be traced to her as cook in households where the disease appeared. It is obvious, therefore, that chronic carriers, as well as persons suffering from mild and unrecognized forms of typhoid fever, may be especially dangerous to the community.

The experiments of Metchnikoff and Besredka[3] indicate that of the lower animals, the chimpanzee alone is susceptible by feeding to a true typhoid infection comparable to that occurring in man. In small animals inoculations produce a general septicemia, but no characteristic lesions.

*Modes of Infection.*—Water plays an important part in the dissemination of the disease and the majority of large epidemics may be traced to the use of drinking water into which typhoid bacilli have found their way from privies, cesspools or the subsoil. Improvement in the water-supply of a community is almost invariably followed by a marked decrease in the general incidence. The death-rate per 100,000 population in the 9 largest cities of the United States between the years 1906 and 1910 averaged 26.5 per cent.; in 1917 it was only 6.2. This reduction in mortality is to be ascribed largely to purification of the water-supplies by filtration or chlorination. In Philadelphia the morbidity fell off 80 per cent. almost at once upon the installation of a filtration system.

Food is a frequent source of infection. Thus milk, originally pure, is often contaminated on its way to the consumer. There is no doubt that the increasing use of pasteurized milk in large cities has had some share in reducing the general incidence of the disease. Ice-cream and butter have been known to carry the infection. Other foods that may be eaten raw, such as oysters "fattened" in polluted streams, and lettuce, celery, water-cress, etc., grown in contaminated soil or washed with contaminated water, sometimes convey the disease. Doubtless flies often act as mechanical carriers of the infection, especially in rural localities and in camps. The bacilli may cling to the body of the insect or be carried in its intestinal contents, and later be deposited on food.

[1] Jour. Amer. Med. Assoc., Oct. 31, 1914.
[2] Jour. Amer. Med. Assoc., June 15, 1907.
[3] Ann. de l'Inst. Pasteur, Mar. 25, 1911.

Typhoid fever is not contagious in the sense that the mere presence of a susceptible person in the vicinity of a patient is dangerous; nevertheless the disease is often spread by personal contact, the bacilli being transferred directly from the excreta of a patient or a healthy carrier to the fingers or food of the one attacked. The influence of contact infection is especially observed where many persons are collected together, as in military camps, in asylums, and in hospitals among the nurses, orderlies, laundry employees, etc., but it is seen also to some extent in private households. Not rarely epidemics brought about in other ways are continued by contact infection. Many instances[1] are on record in which laboratory workers have become infected accidentally in handling pure cultures of typhoid bacilli. Usually the infection occurred in making Widal examinations.

As typhoid bacilli can withstand drying to some extent, it is likely that dust may be a means by which food is contaminated and the disease is transmitted. It is possible, although it has not been proved, that infection by dust may also occur by way of the respiratory tract.

**Morbid Anatomy.**—The characteristic lesions of typhoid fever are found in the lymphoid structures of the intestines—Peyer's patches and solitary nodules—in the mesenteric nodes and in the spleen. In the intestines the changes are most evident in Peyer's patches, although exactly the same process is at work in the solitary nodules. In the first few days the patches acquire a reddish-gray color and become elevated above the surrounding mucosa. The largest of them may be more than a quarter of an inch in thickness. Later, usually early in the second week, the swollen patches lose their reddish-gray color, become pale and opaque, and soften. Still later, at the close of the second week, in most cases, they undergo complete necrosis with the formation of greenish-brown sloughs. In the third week these sloughs are detached and discharged into the lumen of the bowel, leaving ulcers with slightly swollen edges and fairly smooth bases. When the whole patch is destroyed the ulcer is usually ovoid with its long diameter lengthwise of the gut. The floor of the ulcer may be formed by the muscular coat or the peritoneum. Intestinal hemorrhage and perforation are frequent complications. When the ulceration leads to perforation diffuse peritonitis is the usual result, but occasionally the opening in the bowel is closed by adhesions. In cases which go on to recovery healing begins in the fourth week and extends, as a rule, over a period of about two weeks. In some cases the glandular elements are regenerated and the original appearance is restored, but not infrequently the site of the ulcer may be recognized for years by the presence of a smooth, pigmented and depressed scar. Cicatricial contraction does not occur. In mild cases the stage of ulceration may not be reached, the accumulated cells being removed by degeneration and absorption without rupture of the nodule. The chief site of the lesions is the lower end of the ileum, but the vermiform appendix, which is rich in lymphoid tissue, is often involved and sometimes the solitary nodules of the colon are also invaded. The mucous membrane of the affected portion of the intestines usually shows the signs of an acute catarrhal inflammation. The mesenteric lymph-nodes undergo changes similar to those occurring in the intestinal nodules, and in occasional instances they suppurate and rupture into the peritoneum. The spleen is enlarged, of a dark red color, and in the later stages extremely soft. Necroses take place in the pulp just as they do in Peyer's patches and in the mesenteric nodes, and very rarely rupture of the organ ensues with an extravasation of blood into the peritoneal cavity.

The exact nature of the process is not fully understood. The swelling of

[1] For cases see Kisskalt: Zeitsch. f. Hyg., 1915, lxxx.

the lymphoid structures of the intestines, and also of the mesenteric nodes and spleen, depends chiefly upon the presence of numerous large pale cells, with marked phagocytic properties, many of them containing two or three lymphocytes. The origin of these macrophages has been the subject of much discussion. According to Mallory,[1] who has made a very careful study of the lesions, they are derived from the endothelial cells of the blood- and lymph-vessels. He claims that the essential lesion in typhoid fever is a diffuse proliferation of endothelial cells, which is especially marked in the lymphoid tissue of the intestines, but which occurs also to a varying extent in the lymphatic and blood capillaries throughout the body. This change, he believes, is brought about by a diffusible toxin derived from the bacilli. The cause of the necrosis occurring in the hyperplastic tissue is not definitely known. According to some writers it is due to anemia produced by pressure of the proliferated cells on the blood-vessels; others attribute it to the toxic action of the bacilli, and Mallory ascribes it to anemia the consequence of occlusion of the smaller vessels by proliferated endothelial cells and secondary fibrinous thrombi.

In addition to the characteristic lesions that have just been described, others often occur, the cause of which may be the general typhoid septicemia or a secondary infection with pyogenic organisms. The liver, heart and kidneys present the usual evidences of cloudy swelling. The liver may also show many minute areas of necrosis depending upon the destruction of groups of liver cells or of compact masses of macrophages that have reached the liver through the portal streams. A catarrhal or suppurative inflammation is often present in the gall-bladder. The bronchi are frequently the seat of catarrhal inflammation and the lungs of hypostatic congestion. Lobular or lobar pneumonia and pleurisy may also occur. Cases of apparently primary typhoid pneumonitis are occasionally observed. Changes in the bone-marrow are almost constantly present. They consist of congestion, lymphoid hyperplasia, the presence of many large phagocytic cells, a marked paucity of granular myelocytes (the precursors of the polymorphonuclear leucocytes) and disseminated foci or necrosis (Longcope). Hyaline degeneration of the muscles, especially of the recti abdominis, is often found, and very rarely this change is followed by rupture of the affected muscle and hemorrhagic extravasation. Suppurative inflammation may occur in various parts of the body, not only during the course of the disease, but long after recovery. Occasionally septicemic forms of typhoid fever are observed in which there are no characteristic lesions in the intestines or elsewhere, the only changes present being those that have arisen from the general toxemia.

**Symptoms.**—The student must be prepared to meet with many departures from the average clinical picture, as the symptoms vary remarkably in different outbreaks of the disease and also in different individuals. The *period of incubation* is usually about two weeks, but it may be as short as four or five days or as long as three weeks. During this period the patient may be in his usual state of health or he may complain of lassitude, a sense of fatigue, headache, anorexia and disturbed sleep. These prodromal symptoms commonly merge imperceptibly into those of the actual invasion. Although the disease may begin more or less suddenly, especially in children, its onset ordinarily is so insidious that it is difficult to date accurately the commencement of the attack. General malaise, headache, backache, chilliness, anorexia, abdominal pains, and cough are in most cases the earliest manifestations. Epistaxis is also common. Slight diarrhea may be present or there may be marked constipation. The stomach is usually retentive, but

[1] Jour. of Exper. Med., iii, 1898.

vomiting is by no means rare. The occurrence of fever is a very definite indication that the invasion has actually begun.

During the *first week* of the established disease the headache is usually persistent and severe. The patient is feverish, thirsty, and apathetic, although inclined to be restless, especially at night. The temperature rises gradually, reaching its maximum (103° to 104° F.) in most cases at the end of the week. While it is lower in the mornings than in the evenings, it is slightly higher each day than at a corresponding time the day before. The respirations are moderately accelerated; the pulse is increased in frequency, but not, as a rule, in proportion to the increase of temperature; the tongue is moist and covered with a whitish fur, and the breath is fetid. The skin is usually dry, but from time to time there may be profuse sweating, followed by outbreaks of sudamina. Cough, with scanty tenacious expectoration, sometimes slightly blood-streaked, occurs in about one-half of the cases. The abdomen is somewhat distended and pressure in the right iliac region may elicit tenderness and gurgling sounds. Diarrhea with thin yellowish-brown stools is often present. The spleen is enlarged and occasionally tender on palpation. There is at this time rarely any delirium, but the mental processes are slow and slight confusion is sometimes observed at night. The hearing is often decidedly dull. The urine is scanty, high colored, and of high specific gravity, and in many cases gives the diazo-reaction. After the first few days of fever a blood examination usually shows a subnormal leucocyte count or at least an absence of leucocytosis.

With the exception of the headache, which usually has subsided, the symptoms in the *second week* become aggravated. The temperature remains high and presents a more uniform course, although still marked by daily remissions. The tongue tends to become dry and red, and when protruded is often tremulous. The spleen is now considerably enlarged. The expression is dull and heavy, the face is pale and the cheeks are slightly flushed. In severe cases delirium, usually low and muttering but occasionally loud and violent, frequently supervenes. Early in the second week, in most cases between the seventh and the ninth day of the disease, the characteristic rash appears. It consists of small, rounded, slightly elevated rose-colored spots, that disappear on pressure and quickly return when the pressure is removed; the spots are usually confined to the abdomen, chest and back, but they may occur on the limbs and even on the face. They do not appear all at once, but come out in successive crops, each spot lasting three or four days and then fading, leaving sometimes a brownish pigmentation. The spots continue to come out over a period ranging from a few days to two or three weeks. The number present at one time varies from three or four to two hundred or more. An examination of the patient's blood at this time shows in addition to a low leucocyte count a moderate degree of anemia. The Widal reaction, too, is usually positive.

In the *third week* the symptoms may continue without any decided change, they may gradually subside, or they may increase in severity. In the last event, weakness and emaciation become prominent features and a state of profound toxemia usually supervenes. The temperature is continuously high, the pulse is rapid and feeble, the tongue is dry and brown and often fissured, sordes collect on the lips and teeth, and delirium is constantly present. Other nervous symptoms, such as trembling of the limbs, twitching of the muscles (subsultus tendinum), aimless picking at the bedclothes (carphologia), and retention of urine or involuntary discharge of urine and feces, may also occur. The abdomen is sometimes greatly distended and diarrhea may be persistent. In very severe cases the patient often lies on his

back in a somnolent or stuporous condition, so relaxed and exhausted that the attentions of the nurse are constantly required to prevent him from slipping down in the bed. In this week perforation of the bowel, intestinal hemorrhage and pulmonary complications, especially hypostatic congestion, are likely to occur.

With the *fourth week* in ordinary cases comes a gradual improvement in the patient's condition. Defervescence sets in and is usually completed by the end of the week or soon thereafter. Throughout the lysis the temperature frequently shows large daily excursions and marked irregularities. Rarely the fever terminates by crisis. As the temperature falls the general and local symptoms slowly abate, and the appetite and strength improve. The progress of convalescence is, however, slow and often many weeks or even months elapse before the patient regains his former health. Recrudescences of fever lasting two or three days frequently occur during convalescence and not rarely when all danger seems to have been passed, a true relapse takes place, reproducing all the characteristic features of the primary attack.

The Onset.—A sudden onset with unusual symptoms is occasionally observed. Thus, the attack may be ushered in with all the signs and symptoms of ordinary *pneumonia*, the intestinal and other manifestations developing later (pneumotyphoid). Indeed, the disease may run its course without exciting suspicion that any condition other than pneumonia is present. More rarely the initial symptoms suggest a simple *catarrhal affection* of the *tonsils, larynx or bronchi*. In other cases the disease begins with intense headache, vomiting, photophobia, retraction of the head and other symptoms indicative of *meningitis*, and several days may elapse before the true nature of the condition becomes apparent (meningotyphoid). In a few instances actual meningitis due to the typhoid bacillus has occurred without the usual intestinal lesions of typhoid fever. Occasionally the onset is with convulsions or maniacal delirium. In some cases pain and tenderness in the right iliac region are so marked and the onset is so acute that the illness is thought to be *appendicitis*. An exceedingly rare form is one in which the disease begins with all the symptoms of *acute nephritis*, except that the temperature is, as a rule, relatively high (nephrotyphoid).

The Temperature.—The temperature curve shows many variations. In some cases the diurnal remissions are pronounced amounting to two degrees or more; in others they are very slight. Temperatures between 105° and 106° F. are not uncommon at the height of the disease and occasionally the maximum may be 107°, 108° or even 109° F. On the other hand, the temperature may at no time reach 102°, and very rarely, especially in old persons, the attack for the most part is afebrile. Sudden changes in the temperature are suggestive of some complication, although they may admit of other explanations. After a profuse hemorrhage there may be a drop of 8° or even 10°. Perforation is sometimes, but by no means invariably, accompanied by a decided fall. Occasionally, collapse with subnormal temperature ensues without demonstrable cause. Toward the close, when the fever is subsiding, the temperature during the remissions may fall as low as 97° F. With the Brand bath, too, the fall may be considerable. During convalescence persistent *hypothermia* is often observed, but it is of no special significance. Sudden elevations of temperature in the course of the disease usually indicate some secondary infection, such as pneumonia, localized abscess, etc. During convalescence, *recrudescences of fever* lasting two or three days are common. They are to be ascribed in many cases to dietetic errors, constipation or excitement. In some instances, although no compli-

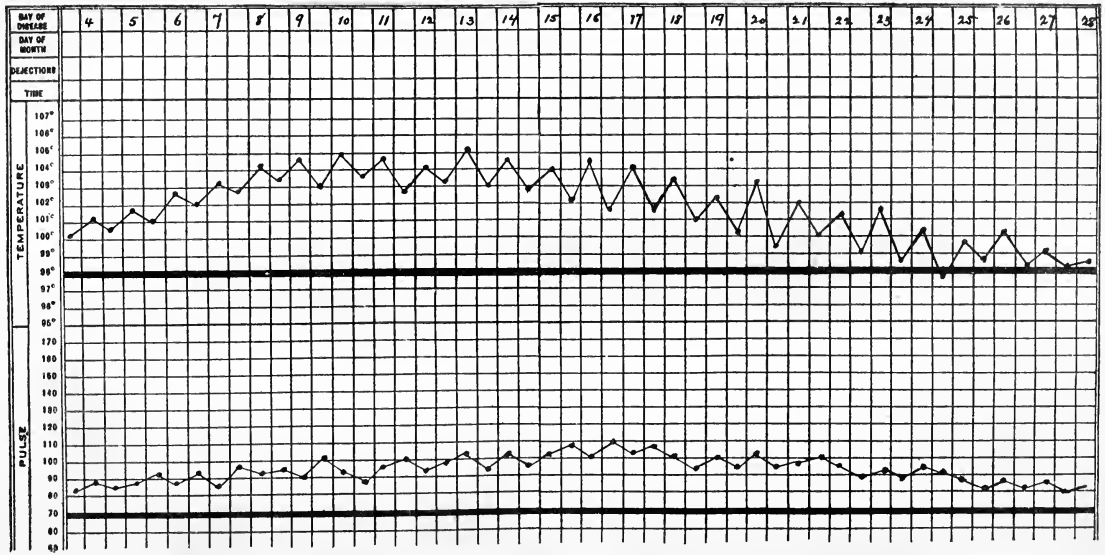


FIG. 3.—Temperature curve of a mild uncomplicated case of typhoid fever. Admission on 4th day.

cations are present, fever persists for a long period, the fourth, fifth or even the sixth week passing before the temperature falls to normal. Occasionally during convalescence, with everything else apparently normal, the temperature rises daily to 99° or 100° F. for a period of two or even three weeks. Such subfebrile states may be disregarded if careful scrutiny reveals no signs of localized infection and the patient's appetite and strength are steadily improving.

Chills are not very uncommon. They may occur at the onset, at intervals during the course of the disease, or during convalescence. Although it is often impossible to assign any cause for them, their occurrence, except at the onset, should always arouse suspicion of some complication, such as pneumonia, phlebitis, otitis media, perforation, abscess, or coexisting malarial fever.

The basal metabolism during the febrile period is considerably increased, the elevation corresponding roughly to the degree of temperature. In some cases the rate is more than 50 per cent. above normal.

Digestive System.—*Vomiting* sometimes occurs at the onset, but it usually ceases after the diet has been properly regulated. Occasionally, however, it persists and seriously interferes with the nourishment of the patient. Late in the disease it may be the result of peritonitis or erosion of the stomach. Hematemesis is rare, but not unknown. *Abdominal pain* is present at some period of the disease in a large proportion of cases. It may be due to colic, the result of diarrhea, constipation, flatulence, or improper feeding. It often accompanies intestinal hemorrhage. When sudden and sharp it should suggest the possibility of perforation. It may depend upon conditions not directly connected with any intestinal disturbance, such as cholecystitis, iliac phlebitis, appendicitis, engorgement of the spleen, pneumonia, pleurisy, etc.

The older writers regarded *diarrhea* as an almost constant symptom. At present, it occurs in less than one-half of the cases. The diarrheic stools vary in number usually from two to twelve in the twenty-four hours. They are thin, very offensive and often of the color and consistency of pea-soup. *Constipation* is almost as frequent as diarrhea, and occasionally, especially in children, it results in fecal impaction. The gurgling often observed in the right iliac fossa is in no way characteristic, as it occurs also in simple catarrhal enteritis. *Tympanites* is a frequent symptom, and, generally speaking, is most marked in severe cases. It may favor the occurrence of perforation or by interfering with the action of the diaphragm may cause dyspnea or cardiac embarrassment. It probably depends more, as a rule, on the general toxemic than on the specific intestinal lesions.

*Intestinal hemorrhage* occurs in from 3 to 8 per cent. of the cases. It may be observed as early as the fifth or sixth day, in which case it is usually slight and probably due to intense congestion of the bowel. Most commonly it occurs in the third or fourth week and is then usually the result of the intestinal ulceration. As a rule, its occurrence is independent of any known exciting cause. In some cases it is associated with prolonged coagulation time of the blood, and very rarely the intestinal bleeding is but a part of a general hemorrhagic tendency. The amount of blood lost varies from a few cubic centimeters to a liter or more, and the hemorrhage may occur once or repeatedly. Profuse bleeding is indicated by a sudden fall of temperature, pallor, sweating, a rapid feeble pulse and extreme prostration. In some instances these symptoms suggest the occurrence of hemorrhage before the blood appears in the stools. Blood that has been retained in the bowel for some time before being evacuated is usually dark, partly clotted

or tarry, and fetid. Single hemorrhages, even if large, are not necessarily dangerous, indeed, they sometimes prove beneficial, but repeated hemorrhages are always cause for anxiety. Of all patients who have hemorrhages, however, probably not more than 20 per cent. succumb to the bleeding.

*Perforation* occurs in from 2 to 4 per cent. of all cases, the incidence varying in different years and in different epidemics. It is responsible for from one-fourth to one-half of all deaths from the disease. It is more frequent in males than in females and is comparatively rare in children. It is most often observed in the third week, but it may take place at any period of the disease, even during convalescence or relapses, and occasionally it occurs before the patient is ill enough to take to bed. Although it is not infrequent in mild attacks, it is more common in severe ones, especially in those with marked abdominal symptoms (diarrhea, tympanites and hemorrhage). The site of the perforation in the vast majority of cases is in the lower portion of the ileum; the next most frequent sites are the colon and the appendix. As a rule only one opening is present, but there may be several. In nearly every case sharp pain is the first symptom. It may be colicky or persistent, and is situated most frequently in the lower right quadrant of the abdomen, but it may be in any of the quadrants, and rarely in males it is referred to the end of the penis. Occasionally it is so slight that for a time it attracts little or no attention. Concurrent with the pain there is often a change of countenance, the features becoming pinched and the expression anxious. Chills, vomiting, hiccough and sweating are frequent symptoms, but are of little significance unless accompanied by corroborative signs. The temperature changes are variable. A sudden drop is sometimes observed, but more frequently there is a moderate elevation followed by a fall. In the vast majority of cases there is a prompt increase in the pulse-rate. An increase in leucocytes usually occurs, although it is not rarely of short duration. Tenderness is present in nearly all cases and this is true also of muscular rigidity. Obliteration of the liver dulness is sometimes noted, but it has little significance if the abdomen is distended, as is usually the case. Other evidences of peritonitis, such as the Hippocratic facies, thoracic breathing, abdominal cyanosis, peritoneal frictions, absence of peristaltic sounds, and movable dulness, appear sooner or later. The conditions that are most likely to be mistaken for perforation are pneumonia or pleurisy with referred abdominal pain, appendicitis, severe colic, hemorrhage, and peritonitis from other causes. Occasionally, *peritonitis* is brought about by the diffusion of bacteria through the intestinal wall without perforation, and rarely it occurs as a result of rupture of a suppurating mesenteric lymph-node, rupture of the spleen, or rupture of a localized abscess.

Simple *appendicitis* or appendicitis with specific typhoid lesions is not very uncommon and may proceed to perforation. In a few instances typhoid infection seems to have been limited to the appendix.

*Jaundice* occurs in from ½ to 2 per cent. of the cases. It is usually a result of catarrh of the bile-ducts or gall-bladder, but it may be due to suppurative cholangitis or cholecystitis, suppurative pylephlebitis, abscess of the liver, or general toxemia. Typhoid bacilli are not only present in the gall-bladder in nearly every case of the disease, but they frequently remain in the viscus for an indefinite period after recovery. It is possible, but not proved, that relapses are often due to re-infection from the gall-bladder, and it seems to have been established that the gall-bladder is the usual habitat of the infecting organisms in so-called typhoid carriers. Infection of the bile may lead to acute cholecystitis of varying degrees of intensity during the course of typhoid fever or it may remain latent for months or years after recovery

and then give rise to acute or chronic cholecystitis. *Acute cholecystitis* was observed clinically in 18 of 1200 cases of typhoid and in 2 it resulted in perforation of the gall-bladder. As a sequel of typhoid infection chronic cholecystitis is especially important because it not infrequently leads to the formation of gall-stones.

Suppurative pylephlebitis, suppurative cholangitis and abscess of the liver are rare complications.

Other complications of the digestive tract are sometimes observed. *Sore throat* is common and occasionally ulcerative or pseudomembranous pharyngitis occurs. In a series of 1200 cases of typhoid fever there were two instances of phlegmonous pharyngitis (Ludwig's angina). Stomatitis or glossitis may ensue. Noma is an infrequent complication. *Parotitis*, usually unilateral, and sometimes ending in suppuration, occurs in about 1 per cent. of the cases. The gland may be invaded from the mouth by way of Stenson's duct or through the blood. Ulceration of the esophagus rarely occurs and a few instances of esophageal stricture following typhoid fever have been recorded.

Skin.—There is no relation between the number of *rose spots* and the severity of the attack. The eruption fails to appear in about 20 per cent. of the cases, being more often absent in children than in adults. In some instances the spots are capped by minute vesicles, and occasionally they are hemorrhagic. Other eruptions are sometimes observed. Miliaria and sudamina are common. Occasionally urticaria, purpura or a rash suggesting measles or scarlet fever appears. Herpes is rare. *Furunculosis*, usually the result of a secondary infection, is not infrequent in the later stages of the attack. With careful nursing *bedsores* may usually be avoided, but occasionally they develop in debilitated patients even though every precaution is taken. *Abscesses* of the subcutaneous tissue or muscles occur in a small proportion of cases. *Facial erysipelas* occasionally supervenes and very rarely superficial gangrene of the skin is observed.

*Falling of the hair* is a common sequel, but permanent baldness is exceptional. As in other fevers the nails often present transverse ridges after recovery, and following prolonged attacks white scar-like lines (lineæ atrophicæ) are sometimes found in the skin, especially about the knees and over the lower portion of the abdomen.

Circulatory System.—The *pulse* in typhoid fever is not characteristic, but it is more frequently dicrotic than in any other febrile disease, and in the first week the rate is often less than would be expected from the fever. As the disease advances the frequency of the pulse increases and the beat becomes smaller and less forcible. Generally speaking, a pulse-rate above 140 in an adult is of bad omen, and particularly so if it is associated with arhythmia. A sudden increase in the pulse-rate often indicates some complication, although it may be due merely to emotional excitement. During convalescence *bradycardia* is not uncommon and need not cause anxiety. Sometimes for several weeks the rate does not exceed 60, 50, or even 40 per minute.

*Degenerative changes in the heart muscle* are common. If slight, the cardiac weakness may be shown only by increased rapidity of the pulse, lowering of the bloodpressure, feebleness of the first heart sound, and, perhaps, a faint systolic murmur at the apex; but if it is marked there may be irregularity of the pulse, gallop rhythm, embryocardia, dilatation of the heart, etc. *Endocarditis* and *pericarditis* are very rare. *Venous thrombosis* occurs in from 2 to 3 per cent. of the cases. It usually affects the femoral vein (left) or one of the other veins of the leg and causes local pain and swelling, and

frequently, also, an increase in the temperature and a leucocytosis. The thrombosis probably depends, as a rule, on a local phlebitis, although weakness of the circulation may be a contributing factor. Recovery nearly always ensues, but convalescence is usually retarded, and for years, in many cases, the affected limb is weak and shows a tendency to swell, especially if much used in standing. Occasionally a portion of a thrombus becomes detached and is carried to the lung. *Arterial thrombosis*, due to a primary arteritis or to the lodgment of an embolus, is very rare. It usually involves the arteries of the lower extremities and is often followed by gangrene. In 1904 Ricketts[1] collected from the literature 134 cases of typhoid fever with gangrene of the lower extremities. *Embolism of the pulmonary* artery may be a cause of sudden death. *Infarcts of the internal organs*, especially of the spleen, are not very uncommon, and may result from arterial thrombosis or embolism. Thayer's[2] studies of the condition of the arteries and heart in 183 persons who had passed through typhoid fever indicate that the disease is capable of playing an important part in the etiology of *arteriosclerosis* and of *retrograde cardiac changes*.

Blood and Hemopoietic Organs.—In the absence of complications, *leucopenia* (5000 to 4000) is the rule after the first week, the degree bearing some relation to the severity and duration of the attack. Occasionally the number of leucocytes may be only 1000. With the leucopenia there is a diminution in the number of polymorphonuclear neutrophils and of eosinophils and an increase in the number of lymphocytes. The eosinophils often entirely disappear. The cause of the low leucocyte count is not definitely known. It may be due to negative chemotaxis or possibly to the changes in the bone-marrow. Transient leucocytosis without any marked change in the differential count sometimes occurs after cold baths, and leucocytosis with an increase in the polymorphonuclear forms is often observed with hemorrhage, with perforation, and especially with secondary infection (abscesses, pneumonia, phlebitis, cholecystitis, etc.).

As the disease progresses both the hemoglobin and the number of red cells undergo a steady reduction, and occasionally in protracted cases a very severe anemia is eventually produced.

The blood-serum agglutinates the typhoid bacillus (*Widal reaction*) at some period of the disease in more than 90 per cent. of the cases. The reaction may be obtained, as a rule, at the end of the first week, and although it sometimes disappears early in convalescence, it often persists for months or even years after the attack. Ordinarily, general clumping of the bacilli within an hour by serum diluted 1 to 50 is regarded as a positive result. Repeated examinations are not rarely necessary, as the reaction is sometimes intermittent and occasionally it fails to appear until very late in the attack or even until a relapse occurs. The test is nearly always positive after prophylactic inoculations of typhoid vaccine, appearing in about ten days after the first dose and persisting for 6 months to 2 years. It is sometimes positive in paratyphoid infections (not often with high dilutions) and in Weil's disease, and occasionally it is present in cases of jaundice. Typhoid bacilli may be isolated from the blood in a large proportion of cases (probably 75 per cent.). In contrast with the Widal reaction, the value of the blood culture in diagnosis decreases as the disease progresses, the bacilli being found most frequently during the first week and often disappearing in the later stages of the infection.

The *spleen* is nearly always swollen and in about two-thirds of the cases

[1] Buffalo Med. Jour., Jan., 1904.
[2] Amer. Jour. of the Med. Sci., Mar., 1904.

the organ is palpable. Abscess of the spleen is a rare complication. In 1911 Melchior[1] collected 13 cases of spontaneous rupture of the spleen in the course of the disease. The *superficial lymph-nodes* throughout the body are sometimes enlarged.

Respiratory System.—*Epistaxis* is common at the onset, especially in children and young adults. *Bronchitis* is also an early feature in the majority of cases, and in some instances it is attended by severe cough. *Catarrhal laryngitis* is not infrequent, and occasionally extensive ulceration of the larynx or perichondritis with exfoliation of the cartilages occurs. The ulcerative lesions of the larynx often develop so stealthily that they escape recognition until edema ensues and seriously endangers the life of the patient. Pneumonia in one form or another occurs in many of the more severe cases. Ordinary *lobar pneumonia* is somewhat infrequent. Usually it is due to the pneumococcus, but the typhoid bacillus may be the causative agent. In rare instances the disease is ushered in with lobar pneumonia. *Lobular pneumonia* occasionally develops early in the disease, but much more frequently it is observed as a terminal event. In stuporous patients it is sometimes brought on by the aspiration of infective foreign material into the bronchi. It may be due either to pyogenic organisms or to the typhoid bacillus. *Hypostatic congestion of the lungs* often occurs in the later stages of typhoid fever and is likely to be overlooked unless the lungs are frequently examined. It is revealed by dulness on percussion and by numerous moist râles and feeble breath sounds on auscultation. A low grade pneumonia often supervenes. *Infarction of the lung* is sometimes observed and very rarely abscess or gangrene occurs consecutive to infarction or pneumonia.

*Pleurisy* is uncommon, but it may occur at any period of the disease either as a primary condition or secondary to some pulmonary lesion, such as pneumonia or infarction. It is usually fibrinous, but it may be serofibrinous or purulent, and in a few instances the effusion has been hemorrhagic. The typhoid bacillus alone may be found in the exudate, but as a rule other organisms are present.

Nervous System.—In many cases dull headache, disturbed sleep, slight deafness and mental hebetude are the only nervous symptoms. In severe attacks, however, there is *delirium*, especially at night and in still more severe attacks other nervous phenomena, such as stupor, tremors, subsultus tendinum and carphologia frequently supervene. Apart from the ordinary delirium, definite psychoses are sometimes observed. They may appear at any stage of the disease and may depend on the specific infection, the pyrexia, or the secondary asthenia. Doubtless individual predisposition may also play a part. At the onset there may be a confusional state or an outbreak of mania. During the course of the disease delusions or hallucinations are not uncommon. Occasionally there is maniacal delirium. The *psychic disorders* that develop during convalescence may take the form of slight mental insufficiency, isolated delusions or hallucinations, mania, melancholia or actual dementia. Isolated delusions or hallucinations and slight mental insufficiency almost invariably disappear, but other forms of post-typhoidal insanity sometimes persist. *Convulsions* are very infrequent. They may be due to some cerebral complication (meningitis, encephalitis, hemorrhage, thrombosis, etc.), to uremia, to epilepsy, to hysteria, or to the specific intoxication itself.

Meningeal symptoms—intense headache, delirium, photobobia, retraction of the head, Kernig's sign, etc.—are not very uncommon. They may denote an actual meningitis, serous or purulent, but much more frequently they are

[1] Centralbl. f. d. Grenzgeb. d. Med. u. Chir., 1911, xiv.

the expression of a toxic condition—the so-called meningism of the French writers. The findings of lumbar puncture are of great value in establishing an exact diagnosis. *Neuritis* is somewhat frequent. Apparently the most common form is that known as "tender toes" (Osler), although this phenomenon has been ascribed by Conner to phlebitis in the small veins of the feet. It is characterized by severe pain and extreme sensitiveness in the tips of the toes and plantar surfaces of the feet. *Polyneuritis*, usually confined to the lower extremities, and inflammation of single nerves, such as the sciatic or ulnar, may also occur. *Hemiplegia* is rare, and has been observed most frequently in children. In 1907 Smithies[1] collected 40 cases. It is usually the result of thrombosis of the middle cerebral artery, but it may be due to hemorrhage, embolic softening or encephalitis. Among other very rare nervous complications may be mentioned acute myelitis, bulbar palsy and cerebral abscess.

Organs of Special Sense.—Temporary deafness and tinnitus aurium are of frequent occurrence, especially at the onset. *Otitis media* occurs in from 1 to 3 per cent. of the cases. With the exception of *catarrhal conjunctivitis*, which occurs in many cases, ocular complications are comparatively rare, but keratitis, iritis, choroiditis, retinal hemorrhage, optic neuritis and paralysis of the intraocular or extraocular muscles have been noted.

Genito-urinary System.—*Retention of urine* is common both at the onset and later after the occurrence of stupor. In severe cases incontinence of urine, with or without partial retention, is also frequently observed. The *urine* is usually scanty, dark-colored, of high specific gravity until about the fourth week, when in favorable cases it becomes copious and pale, and its specific gravity falls. Even in the early stages, however, polyuria may often be produced by the administration of large amounts of water. The diazo reaction is usually present, but as it occurs in a number of other febrile diseases it cannot be considered characteristic. *Typhoid bacilluria* is present in the later stages of the disease in about one-fourth of the cases, and sometimes it persists for months or even years. Slight *albuminuria* with a few tube-casts is very frequently noted, but actual nephritis is not common, and when it does occur it rarely gives rise to dropsy or to uremia and usually subsides if the typhoid infection ends favorably. *Cystitis* or *pyelitis* due to the typhoid bacillus or to infection with pyogenic organisms occurs in a small proportion of cases. *Menstruation* often ceases during the course of the disease and in some cases does not appear for several months following the attack. On the other hand, it may occur prematurely at the onset and be profuse. *Pregnancy* is unfavorably affected, abortion or premature labor occurring in at least two-thirds of the cases (Vinary, Martinet, Penot, Sacquin). If premature labor occurs the child is usually still born or dies soon after birth, generally from the transmitted infection in the form of a typhoid septicemia without gross intestinal lesions.

Endocrinous Glands.—*Orchitis* is a rare complication, occurring, as a rule, during convalescence. In most cases it lasts about two weeks and terminates in resolution, although suppuration or atrophy of the testicle may occur. Suppuration of ovarian cysts after typhoid fever has been noted in a few instances. Acute thyroiditis, simple or suppurative, rarely develops during convalescence. In Gali's case[2] typhoid bacilli were obtained from a thyroid abscess 21 years after an attack of typhoid fever.

Muscles, Bones and Joints.—*Rupture of the rectus muscle* of the abdomen has been noted in a few instances. A hematoma is usually formed and

[1] Jour. Amer. Med. Assoc., Aug. 3, 1907.
[2] Berlin. klin. Woch., 1914, li, No. 50.

in 16 of the 35 cases collected by Perochaud[1] there was secondary suppuration. *Lesions of the bones*—periosteitis, osteitis, osteomyelitis—are not very uncommon sequelæ and may occur months or even years after the fever. The tibia, femur, ribs, ulna and humerus are the bones most often affected. Examination of the pus may show a mixed infection or the typhoid bacillus in pure culture. The condition known as "*typhoid spine*" almost always depends on inflammatory changes in the periosteum or bony structure of the vertebræ, usually of the lumbar region. Occasionally, however, it appears to be a neurosis similar to the "irritable spine" that may occur after trauma. It usually appears during convalescence and is characterized by pain in the lumbar region, sometimes radiating down the legs, tenderness and muscular rigidity. Various neurotic or hysterical phenomena, slight fever, muscular wasting and local deformity may also be present. An exact diagnosis may be much facilitated by the use of the x-rays. The condition lasts for from a few weeks to many months and only rarely leads to suppuration.

*Arthritis* is occasionally observed. It may be polyarticular or monarticular. It rarely proceeds to suppuration or to ankylosis, but in the hip joint it is frequently followed by spontaneous dislocation. According to Keen[2] more than half of the cases of typhoid arthritis result in spontaneous luxation, nearly all of which are in the hip joint.

**Varieties.**—Remarkable differences are observed in cases of typhoid fever, both as regards the severity of the attack and the predominance of certain groups of symptoms. *Mild forms* frequently occur in which the course and duration correspond to those of the ordinary type, but in which the symptoms generally are poorly developed. In the form known as *abortive typhoid* the disease begins with severe manifestations, but these soon subside, the temperature becomes normal between the seventh and the fourteenth days, and convalescence is rapid. In the so-called *ambulatory form* the weakness is so slight during the early stages at least, that the patient continues to walk about until a favorable termination is reached, or, more frequently, until the occurrence of some severe symptom or complication, such as persistent diarrhea, intestinal hemorrhage or even perforation, enforces attention. A *malignant form* characterized by high fever, marked prostration, and grave nervous symptoms is sometimes observed. Many of the severe cases are due to secondary infection with pyogenic organisms. *Hemorrhagic typhoid* is a rare but very grave form characterized by a petechial eruption and hemorrhages from the mucous membranes. Occasionally typhoid fever occurs with an unusual localization of the lesions, as in the lung, cerebral meninges, or kidneys, and to indicate the organ chiefly affected the terms *pneumo-typhoid*, *meningo-typhoid* and *nephro-typhoid*, etc., are employed.

Typhoid fever in young children shows some variations from the form usually seen in adults. The onset is, as a rule, more sudden; the temperature generally rises more rapidly and presents more marked remissions; vomiting is more frequent; cerebral symptoms, especially those suggesting meningitis, are often prominent, whereas the abdominal symptoms are likely to be mild; relapses are apparently more frequent, but hemorrhage and perforation are comparatively rare; on the whole the duration is shorter and the mortality less than in adults.

**Relapse.**—This occurs in from 5 to 15 per cent. of all cases, the frequency varying in different epidemics and in different localities. As a rule, the relapse comes on within the first few days of convalescence, but it may appear before the temperature of the primary attack has reached normal (inter-

[1] Gaz. méd. de Nantes, 1905, No. 38.
[2] Surg. Comp. and Sequels of Typhoid Fever, Phila., 1898.

current relapse), and occasionally it does not appear until two or three weeks of apyrexia have elapsed. Recrudescences of fever differ from true relapses in lasting only a few days and in not being accompanied by other typhoidal symptoms. A relapse ordinarily lasts about ten days or two weeks, and is, as a rule, milder and shorter than the primary attack. Exceptions, however, occur; intercurrent relapses in particular sometimes being protracted and severe. There may be a second, a third, a fourth, and even a fifth relapse, in which event the entire process may occupy three or four months. With multiple relapses, each one in turn is often milder and shorter than the one preceding it.

**Diagnosis**.—It is not always possible to make an absolute diagnosis within the first five or six days, but typhoid fever should be strongly suspected, if after a week or more of general malaise there is a gradual rise of temperature without obvious cause, and especially if nose-bleed, enlargement of the spleen, diarrhea, or slight bronchial catarrh is also present. Dicrotism of the pulse, a lower pulse-rate than would be expected from the fever, a listless heavy expression, slight deafness, and a tremulous tongue are also suggestive. Later, the occurrence of a roseolous rash, of leucopenia, of a positive Widal reaction, or of intestinal hemorrhage makes the diagnosis almost certain. No single finding, however, except the isolation of typhoid bacilli from the blood, the stools or the urine, affords indubitable proof of the disease. In doubtful cases, a high leucocyte count, early jaundice, facial herpes, and coryza speak against typhoid fever. The diseases that most frequently cause difficulty in diagnosis are the following:

*Acute Miliary Tuberculosis*.—In this disease there is often evidence of focal tuberculosis; the onset is frequently marked by restlessness and irritability; the temperature is, as a rule, very irregular; the pulse is accelerated out of proportion to the rise of temperature, and is rarely dicrotic; the respirations are likely to be more rapid than in typhoid fever; periodic cyanosis of the lips and finger tips is common and suggestive; rose spots and intestinal hemorrhage, while not unknown, occur very infrequently; the Widal reaction is absent and typhoid bacilli are not found in the blood; although leucopenia is the rule, leucocytosis is more common than in typhoid; tubercle bacilli are sometimes found in the cerebrospinal fluid and tubercles occasionally appear in the choroid.

*Cerebrospinal Meningitis*.—If typhoid fever begins with pronounced cerebral symptoms or with actual meningitis it may readily be mistaken for cerebrospinal fever, but the abrupt onset, irregular fever, absence of rose spots, presence of herpes or perhaps of petechiæ, the occurrence of ocular changes (marked inequality of the pupils, squint, optic neuritis, etc.), and, above all, the results of a bacteriologic and cytologic examination of the spinal fluid will usually make the diagnosis of meningitis clear.

Certain *septicemic processes*, such as ulcerative endocarditis, puerperal septicemia, deep-seated abscesses, small foci of suppuration in the pleura, osteomyelitis, etc., sometimes produce symptoms much like those of typhoid fever, but they may be differentiated, as a rule, by the discovery of a source of infection, by the high leucocyte count, and by the results of blood cultures.

*Ulcerative endocarditis* is usually distinguished with ease. In some cases, however, the source of the infection cannot be detected, the cardiac symptoms are slight, and septic features (sweats, chills, leucocytosis) and embolic phenomena (petechial rash and infarctions) are lacking, and the patient presents only a continued fever with increasing anemia and prostration. Under these circumstances the results of the Widal test and of blood cultures are of paramount importance.

It should not be forgotten that in children, especially a mild continued fever, with but little other disturbance, may be due to otitis media or to infection of the urinary tract with the colon bacillus.

*Pneumonia* and typhoid fever are not rarely confused. A patient may have pneumonia and for a few days the symptoms may resemble those of typhoid fever; pneumonia may develop as a complication in the course of typhoid fever; and, again, typhoid may begin with the symptoms of a lobar pneumonia. *Appendicitis* occasionally causes difficulty. Usually the abrupt onset, rapid rise of temperature, marked local tenderness and muscular rigidity, leucocytosis, absence of splenic tumefaction, etc., leave no doubt as to the diagnosis, but unfortunately typhoid fever sometimes begins suddenly with symptoms resembling those of appendicitis and not very rarely ordinary appendicitis or appendicitis with specific lesions develops in the early stages of typhoid fever.

*Typhus* and typhoid fevers have many features in common. In the former, however, the onset is usually abrupt and often accompanied by severe pain in the back and limbs; the face is bloated and uniformly flushed and the eyes are injected; the temperature reaches its maximum in 3 or 4 days, remains high about ten days, and then falls by rapid lysis; the rash appears about the fourth day, is measles-like and sometimes hemorrhagic, develops rapidly and not in successive crops, and is usually widely distributed; and both the Widal reaction and the blood culture are negative.

The *aestivo-autumnal form of malarial* fever is occasionally misleading, but the presence of the parasites, which will usually be found if the examinations of the blood are made frequently and at short intervals, and the favorable reaction to quinin are sufficient to establish the diagnosis.

*Influenza* may at first suggest typhoid fever, but the presence of an epidemic, the abrupt onset, the course of the fever, and the absence of the rose spots and of the Widal reaction will soon lead to a correct diagnosis.

*Trichiniasis* sometimes resembles typhoid fever in presenting diarrhea, general malaise, continued fever and even a roseolar rash and tumefaction of the spleen. Important points in favor of trichiniasis are a history of raw or undercooked pork having been eaten, the occurrence of leucocytosis with marked eosinophilia, of pronounced muscular soreness and of edema of the eye-lids, and the discovery of trichinæ in the stools or in pieces of excised muscle.

Other conditions causing long-continued fever without definite localizing symptoms and with which typhoid fever is occasionally confused are leukemia, Hodgkin's disease, lymphosarcoma or tuberculosis of the deep-seated lymph-nodes (mediastinal, mesenteric or retroperitoneal nodes); syphilis in both the secondary and tertiary stages; deep-seated carcinoma or sarcoma, particularly certain malignant tumors of the liver; and mild forms of tuberculous peritonitis. In certain localities Malta fever, kala-azar and trypanosomiasis may also cause confusion.

**Duration and Prognosis.**—In favorable cases the average duration of an attack, estimating from the onset to the disappearance of fever, is three or four weeks. In fatal cases death is comparatively rare before the close of the second week. The most frequent cause of death is toxemia. The prognosis is always doubtful, for even in cases that are apparently mild, death from hemorrhage or perforation sometimes occurs without warning, and occasionally there is sudden collapse for which no adequate cause can be found. The death-rate is low in children, but it is relatively high in infants and in persons more than 50 years of age. Coexisting myocardial or renal disease, alcoholism and marked obesity add considerably to the danger. Aside from

hemorrhage and perforation, a pulse-rate persistently above 130 (except in young children), obstinate diarrhea, marked tympanites, pronounced nervous symptoms (muttering delirium, tremors, etc.), especially if they appear early, and hypostatic congestion of the lungs are unfavorable features.

The death-rate varies much in different outbreaks and in different localities, but the average is about 8 per cent. It is higher in hospitals, where many of the patients have come under treatment at a late period, than it is in private practice. As a rule, relapses are less dangerous than primary attacks.

**Prophylactic Measures.**—These comprise the obtaining of a pure water supply, the proper disposal of excreta, precautions against food (especially milk) contamination, protection against flies, the vaccination of all persons who are in special danger of infection, the isolation of the sick, the thorough disinfection of the patient's discharges (feces, urine, sputa) and all articles likely to be soiled by the patient, and constant care on the part of nurses and attendants to protect themselves and others against direct infection.

Public water-supplies, unless obtained from sources that are above suspicion, should be purified by sand filtration or by the relatively cheap chlorination method. Protection against milk-borne typhoid may be easily secured by pasteurizing all milk not known to be safe. During the prevalence of epidemics all drinking water and milk should be boiled and no vegetables or shell-fish should be eaten raw. Vaccination affords protection, as a rule, for two or three years, and is to be strongly recommended in the case of soldiers, travelers, persons much exposed in epidemics, nurses, orderlies, and all others who are in special danger of contracting the disease. The vaccine is given subcutaneously under aseptic precautions in three doses, the first dose (500 million killed bacilli) being followed ten days later by a second dose (1000 million) and after another interval of ten days by a third dose (1000 million). Severe reactions (marked redness and swelling at the site of the injection, malaise, chills, fever, muscular pains, vomiting, etc.) sometimes occur, but are exceptional in persons who are in good physical condition at the time and who abstain from alcohol and avoid muscular exertion and exposure to the sun for twenty-four hours following the inoculation. Pregnancy is a contraindication. In the World War vaccination reduced the typhoid mortality to 0.04 per hundred thousand troops (French and American armies). In previous wars of the last half century the typhoid mortality varied from 11.2 to 21 per thousand troops.

Stools and other excreta of typhoid patients should be thoroughly mixed with twice their volume of a 5 per cent. phenol solution or a 5 per cent. solution of a good preparation of chlorinated lime and allowed to stand for at least two hours. Disinfection of feces and urine should be continued until the third or fourth week of convalescence or, if possible, until several examinations have shown them to be free from typhoid bacilli. After a stool the patient's buttocks should be carefully washed with a disinfectant solution and the cloths used for the purpose should subsequently be burned. Bed-linen, etc., should be soaked in a solution of phenol (5 per cent.) and boiled before being washed. The patient should have his own eating utensils and these should be disinfected after use by boiling. The disinfection of the bath-water is best accomplished by stirring into it about half a pound of chlorinated lime (250 gm.) and allowing it to stand for an hour. Throughout the attack the nurse should wear rubber gloves when giving baths or handling otherwise the patient, or afterward wash the hands thoroughly with hot water and soap and then bathe them in 70 per cent. alcohol.

No satisfactory means of ridding typhoid carriers of their infection has

yet been found. So-called intestinal and urinary antiseptics, such as salol and hexamethylenamin, have been tried, but usually without effecting any permanent benefit. Treatment by autogenous bacterial vaccines seems to offer a slightly better chance of success. In some instances cholecystectomy has given decisive results. Carriers should be under the observation of boards of health and should not be allowed to engage in occupations requiring the handling of food materials.

**Treatment.**—As soon as symptoms of typhoid fever show themselves, even if the diagnosis is in doubt, the patient should be put to bed and kept there until convalescence is well advanced. Hospital treatment offers many advantages, but in many cases it is not essential. It is true, however, "that a good nurse without any doctor is better than the best doctor without any nurse." Whether the treatment is conducted in the home or in the hospital, isolation is essential. Everything that is likely to tire the patient or to disturb his emotions must be avoided, and therefore the fewer the visitors whom he sees the better. The room should be large and airy, and provided with efficient means of securing good ventilation. The temperature of the room should be kept between 65° and 70° F. (18.5°–21° C.). The bed should be moderately firm. The mattress should be protected by a rubber cloth spread beneath the sheet and the latter should be kept smooth to guard against the development of bedsores. Even in mild cases it is advisable to have a nurse or attendant constantly at hand, since accidents resulting from sudden delirium are liable to occur. The use of the bed-pan and urinal must be insisted upon from the beginning. Absolute cleanliness is all important. The position of the patient should be changed from time to time, not only to avoid bedsores but to lessen the tendency to hypostatic congestion of the lungs. Parts that are subjected to pressure should be frequently sponged with alcohol and then freely dusted with talcum powder. After each feeding the teeth should be cleaned and the mouth swabbed out with a saturated solution of boric acid or with such a wash as:

℞. Succi limonis..... f℥i (4.0 mils)
Glycerini..... f℥iii (12.0 mils)
Liquoris antiseptici..... f℥i (30.0 mils)
Aquæ..... q. s. ad f℥ vi (180.0 mils) M.

Heavy coatings on the tongue may be removed by careful scraping with a whalebone bent into a loop.

The food should be liquid or semiliquid, nutritious, and easily digestible, the exact quality and quantity depending on the degree of toxemia and the presence or absence of gastro-intestinal disturbances. Milk alone (3 to 4 pints in 24 hours) does not supply more than one-half of the required number of calories (2500), but, as a rule, it should form a large part of the diet. It may be given diluted with lime water or aërated water, or as buttermilk, malted milk, koumiss, junket, or in part as cream or ice-cream. Among other safe foods may be mentioned raw or soft boiled eggs, strained gruels, milk toast, chicken jelly, tea, cocoa, fruit juices, blanc mange, wine jelly and custard. Beef tea has little caloric value and may even be harmful, but soups of chicken, mutton, veal or oysters, strained and thickened with rice flour are often useful. Three pints of good milk, to which 6 ounces of cream and 6 ounces of milk sugar have been added, together with a soft boiled egg and a dish of rice custard pudding or of strained oatmeal in the twenty-four hours will allow the patient a little more than 2000 calories. If there are signs of gastric disturbance or if diarrhea sets in the diet should be restricted for a

time to whey or albumin water.[1] As a rule, the food should be given in divided quantities every three hours, the patient being aroused at night for nourishment unless his attack is a very mild one or unless he has recently suffered from insomnia.

Water should be given in large amounts between the feedings, the patient being urged to take it even if he has no desire for it. Taken freely, the water stimulates excretion, improves the condition of the mouth, and lessens the nervous symptoms.

Alcohol is not needed in the majority of cases, but when there is evidence of previous intemperance, when the patient is unable to take enough food, and especially when there are indications of severe toxemia it is often of value. Ordinarily the best form of alcohol is whisky or brandy, but occasionally, sherry, port, or champagne may be better borne. At first one or two ounces (30.0–60.0 mils) of whisky in the twenty-four hours may be sufficient; later it may be necessary to increase the amount to 3 or 4 ounces (90.0–120.0 mils) or more. The quantity must be determined in each case by the effect. If the pulse becomes stronger and less rapid, the tongue less dry, the urine more copious, and the mind clearer under the administration of the alcohol, it is doing good; if, however, opposite effects are observed, it is doing harm, at least in the quantity in which it is being employed.

There is ample evidence to show that the mortality of typhoid fever is considerably reduced by the cold-bath treatment, strongly advocated by Brand, of Stettin. To secure the best results the bathing should be instituted early and continued systematically throughout the attack. The details of the treatment are as follows: A portable tub on wheels is kept two-thirds full of water at 70° F. and is rolled to the edge of the bed when needed. Every third hour, if his rectal temperature is 102.5° F. or more, the patient is given a bath lasting about 15 minutes. His ears are plugged with cotton, his clothes are removed, he is wrapped in a sheet, and then he is carefully lifted into the water by two attendants and submerged up to the neck. His head is now supported by a rubber pillow or air-ring and covered by a thick cloth wrung out of cold water.

During the whole period of the immersion cold affusions should be applied to the head frequently, and the back, chest, and extremities should be rubbed vigorously and continuously. As the rubbing increases the stimulating effect of the bath and aids in preventing chill, it should never be omitted. After the bath the patient is lifted in the same way as before and placed on the bed, which in the meantime has been prepared with a large rubber sheet, covered by a blanket. He is then folded in the blanket and hot bottles are placed at his feet. At the end of five or ten minutes the wet sheet and blanket are removed, the patient is rubbed dry, and the gown and bedclothes are replaced. A half ounce of whisky or a small cup of hot coffee may be given before or immediately after the bath, if it seems advisable. The rectal temperature is taken twenty minutes after the bath, and is usually found to have fallen 1° or 2° F. Modifications of the procedure are often desirable or absolutely necessary. Thus, if the patient is very nervous the initial bath may be given at 80°, 85° or even 90° F. or throughout he may be bathed in water of about 90° F., which is gradually cooled down to 75° or 70°. Again, in debilitated subjects, or in patients who are already markedly toxic when first seen it is usually advisable to give shorter baths and to have the temperature of the water higher (75° or 80° F.). The good effects of the

[1]Albumin water is made by shaking together the whites of one or two eggs and a little water, then straining and adding a few drops of orange juice or sherry and perhaps some sugar.

cold baths are: prevention or lessening of nervous symptoms, improvement in the pulse, increased secretion of urine and reduction of temperature. When employed systematically from the beginning, the so-called typhoid state rarely develops. Contraindications to the use of the baths are hemorrhage, indications of intestinal perforation or peritonitis, phlebitis, cholecystitis, great prostration and menstruation. Pneumonia and pregnancy are not contraindications, nor are shivering or cyanosis, unless very prolonged. Collapse, abdominal pain, hemorrhage, vomiting, and extreme cyanosis are indications for immediate removal from the bath.

When for any reason a tub cannot be used a trough may be made in the bed by spreading a large rubber sheet under the patient and elevating its edges on coils of blankets or on sandbags. When the cold baths are not well borne or cannot conveniently be given cold packs or cold sponging may be employed, although they are much inferior to immersion with friction. In applying the cold pack the bed is first protected by a rubber cloth, and then the patient is stripped and wrapped in a sheet wrung out of water at 70°–60° F. After fifteen or twenty minutes he is rubbed dry. During the pack it is well to sprinkle the sheet with cold water. Cold sponging gives comfort to the patient, but has little effect on the temperature or the general condition. Alcohol may be added to the water, which may be at 65° F. or less, and the sponging may be kept up for ten minutes and be repeated every two hours.

**Specific Treatment.**—The use of vaccines in the treatment of typhoid fever is still in the experimental stage. Numerous reports on the subject have appeared during the last few years, but the results as shown by the death rate are not convincing. All observers emphasize the importance of early treatment, and agree that the vaccines, if properly used, at least do no harm. An initial dose of from 250,000,000 to 500,000,000 bacteria (prepared by Wright's method) should be given subcutaneously and followed by two or more larger doses at three-day intervals. Ichikawa[1] has reported striking results from the intravenous injection of sensitized bacteria (a mixture of typhoid bacilli and serum from typhoid convalescents) and Koranyi has confirmed Ichikawa's claims.

**Treatment of Special Symptoms and Complications.**—*Cardiovascular System.*—Cold bathing and the timely use of alcohol do much to guard against heart-failure. When the tendency to cardiac failure is pronounced strychnin may be given in doses of $\frac{1}{40}$ to $\frac{1}{30}$ grain (0.0016–0.002 gm.), subcutaneously or by the mouth, every four hours. Digalen, 10 minims (0.06 mil), or digipuratum, 10 minims (0.06 mil), subcutaneously, three times a day, is sometimes useful. Salt solution (500 c.c. to 750 mils) once or twice a day, by the bowel or subcutaneously, is often serviceable. In threatened collapse camphor, 2 grains (0.13 gm.), in sterile olive oil, or caffein and sodium salicylate, 5 grains (0.3 gm.), may be given into a muscle every two or three hours, or adrenalin, 2 to 3 minims (0.1–0.2 mil) may be given intravenously, and followed by the camphor or caffein.

Phlebitis should be treated by rest of the affected limb in an elevated position and the application of cotton wool and a light bandage. In the early stages an ice-bag over the thrombosis or compresses wrung out of a saturated solution of magnesium sulphate will usually relieve the pain. If there is very severe pain morphin may be required. Later, an ointment of mercury and belladonna may be used. If the limb swells when the patient is up and about an elastic stocking should be worn.

**Nervous System.**—Headache is best treated by the use of the ice-cap. Occasionally a small dose of phenacetin, repeated once or twice, may be

[1] Ztschr. f. Immunit äts. u. exper. Therap., 1914, xxiii.

needed. The general nervous symptoms are best controlled by hydrotherapy. Muttering is usually an indication for alcoholic stimulation. In active or violent delirium morphin alone or in combination with scopolamin may be necessary. Restraint by sheets is sometimes required. Meningism not rarely yields to lumbar puncture. Wakefulness may usually be overcome by a cold pack at night or by the use of bromids, chloral, trional or veronal in moderate doses. When insomnia is prolonged, however, it is advisable to use morphin hypodermically. For tender toes applications of methyl salicylate with 20 grains (1.3 gm.) of menthol to the ounce (30.0 mils) or light paintings with a mixture of tincture of iodine and alcohol (equal parts) are useful.

*Gastro-intestinal Tract.*—Vomiting at the outset usually yields to a reduction of the diet to albumin-water or to the temporary suspension of all feeding. The best sedatives are cracked ice, powders of cerium oxalate, 10 grains (0.65 gm.), or of bismuth subnitrate, 15 grains (1.0 gm.), and tablets of cocain, 1/6 grain (0.01 gm.). A mustard plaster to the epigastrium is sometimes efficacious, and in intractable cases lavage should be tried. If the bowels do not move spontaneously an enema of oil or of soap and water may be given every other day. Except perhaps at the onset, no purgative should be given by the mouth during the febrile period. Diarrhea does not call for intervention unless there are more than 2 or 3 loose stools in the twenty-four hours. In the majority of cases it yields to the temporary substitution of albumin-water for milk and other foods. In some cases, however, it is necessary to give bismuth, 20–30 grains (1.3–2.0 gm.) with codein and an antiseptic, as in the following formula:

℞. Codeinæ sulphatis..... gr. ii–iv (1.3–2.5 gm.)
Phenylis salicylatis..... gr. xxiv (1.5 gm.)
Bismuthi subnitratis..... ℥ss (15.0 gm.) M.
Fiant chartulæ No. xii.
Sig.—One every three hours.

In obstinate cases silver nitrate, 1/4 grain (0.015 gm.), or copper sulphate, 1/2 grain (0.03 gm.), with opium, in pill will sometimes be found useful.

Tympanites may often be relieved by reducing the diet to albumin-water, applying turpentine stupes or cold water compresses to the abdomen, and giving by the mouth oil of turpentine, 10 minims (0.6 mil) in capsules or in emulsion. Saline irrigations and enemas containing asafetida or oil of turpentine are also useful. If extreme, a soft rectal tube may be introduced into the bowel and left in for 15 or 20 minutes. When all these measures fail a subcutaneous injection of pituitary extract (1 mil) or of eserin sulphate, 1/50 grain (0.0013 gm.) may be tried.

Intestinal hemorrhage is best treated by securing absolute rest, withholding food temporarily, applying an ice-bag to the abdomen, and giving morphin hypodermically. Human serum or fresh horse serum (20 to 30 mils) is worthy of trial, especially in repeated or prolonged bleeding. Profound anemia following profuse hemorrhage will call for elevation of the foot of of the bed, and the application of compressing bandages to the arms and legs. The administration of stimulants and the subcutaneous or intravenous injection of salt solution should be withheld unless death from collapse is imminent, as they favor a recurrence of the bleeding. Blood transfusion is preferable to the injection of salt solution, and if feasible should be substituted for the latter when filling of the vessels is imperative.

Recovery from perforation is so very rare under expectant treatment that operative intervention should be urged in all cases in which the patient

is not obviously moribund. Statistics show a recovery rate of at least 25 per cent. in operations done within the first twenty-four hours.

*Urinary Tract.*—Retention of urine may frequently be overcome by the use of hot applications to the abdomen or enemas of hot water. In some cases, however, it is necessary to employ the catheter. For bacilluria, hexamethylenamin, 10 to 15 grains (0.65–1.0 gm.) three times a day, is the best remedy.

*Respiratory Tract.*—The bronchitis, as a rule, may be disregarded. If severe it will require the administration of expectorants, preferably potassium citrate, 20 grains (1.3 gm.) or ammonium chlorid, 5 to 10 grains (0.3–0.6 gm.), three times a day, and, perhaps, small doses of paregoric. Hypostatic pneumonia can be in great measure prevented by hydrotherapy, frequent change of position, and the timely use of stimulants. When developed it is often relieved by the liberal use of dry cups. Ordinary pneumonia is to be treated as it would be if it were primary.

*The Skin.*—Bedsores can usually be prevented by absolute cleanliness, attention to the smoothness and dryness of the sheets, judicious changes of position, frequent applications of alcohol and dusting powder, and the timely use of air-cushions or a water-bed. Slight abrasions may be painted with flexible collodion, or covered with balsam of Peru and then powdered. When there is much difficulty in keeping the parts dry, zinc ointment may be freely applied. Ulcers should be washed with antiseptic solutions, dusted with iodoform or aristol, and then protected by a large piece of soap-plaster. An ointment of balsam of Peru, 2 drams (8.0 gm.), aristol 1 dram (4.0. gm.), and petrolatum, 1 ounce (30.0 gm.), is sometimes very efficacious.

**Treatment of Convalescence.**—As a rule, after the temperature has been normal for a week or ten days the patient may be propped up in bed, and in three or four days more he may be allowed to sit up in a chair. The return to full diet should always be effected very gradually. Tonics, such as iron, quinin and strychnin, are often useful. In many instances a complete change of air and surroundings is advantageous. An abundance of time is necessarily required to repair the damage to the tissues wrought by the disease, hence the patient should be cautioned about returning to his work, whether it is mental or physical, too soon. Permanent impairment of health may not rarely be traced to premature resumption of work.

## PARATYPHOID FEVER

Febrile conditions are frequently encountered which closely resemble typhoid fever clinically, but which differ in the causative bacterial factor. The bacteria concerned are intermediate in their cultural peculiarities between *Bacillus typhosus* and *Bacillus coli communis* and are known as *Bacillus paratyphosus* A and *Bacillus paratyphosus* B (Schottmüller). They were first recognized by Achard and Bensaude[1] in 1896 and first isolated from the blood during life by Gwyn[2] in 1898. The *Bacillus enteritidis* (Gärtner), occurring in meat poisoning is very closely related to *Bacillus paratyphosus* B, but the two organisms apparently do not produce one and the same disease. Unlike paratyphoid fever, which is spread by human carriers, meat poisoning results from the ingestion of food that has been derived from infected animals or that has been contaminated by animal agency. Moreover, the infection that is conveyed by meat usually takes the form of an acute gastro-enteritis of brief duration, whereas infection with the para-

[1] Bull. et mém. Soc. méd. de hôp., Paris, 1896, xiii.
[2] Johns Hopkins Hosp. Bull., 1898, ix.

typhoid organisms usually produces the clinical picture of typhoid fever. It is true, however, that anomalous cases of acute infection caused by *Bacillus paratyphosus* B and of prolonged pyrexia caused by *Bacillus enteritidis* occasionally occur. Of the two paratyphoid organisms A is an acid producer, B an alkali producer. In most countries *Bacillus paratyphosus* B is the prevailing type. The intestinal changes of paratyphoid infections vary from a simple ileocolitis to lesions indistinguishable from those of ordinary typhoid fever. From the clinical point of view there is no radical difference between typhoid and paratyphoid fevers. The differential diagnosis must be made either by cultivating the infecting bacillus from the patient's blood or by special agglutination tests. Speaking generally, in paratyphoid fever the onset is more abrupt, rigors are more frequent, the symptoms are milder, defervescence occurs earlier, and the entire course is shorter than in typhoid fever. Cases of every degree of severity, however, occur, and the milder ones often escape recognition, being diagnosed usually as indigestion, "gastric fever" or influenza. Klein and Torrey[1] draw attention to the frequency with which the symptoms of severer bonchitis or of bronchopneumonia dominate the clinical picture, the sputum in such cases containing the bacillus and probably being a means of spreading the infection.

Paratyphoid fever offers a better prognosis than typhoid fever, the mortality of paratyphoid B ranging between 3 and 5 per cent. and that of paratyphoid A ranging between 1 and 2 per cent.

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## DIPHTHERIA

**Definition.**—Diphtheria is an acute contagious disease excited by Bacillus diphtheriæ, and characterized by the formation of false membrane upon certain mucous surfaces, especially those of the throat and adjacent parts, and by a more or less severe toxemia, the result of the absorption of a poison elaborated by the specific organism at or near the site of the local lesions. The bacilli themselves are for the most part localized in the affected area, but the toxin is widely diffused.

**Etiology.**—Diphtheria is met with in all climates, but is more common in cold and temperate regions than in the tropics. It is endemic in populous centers and at intervals assumes an epidemic character. The majority of outbreaks occur in the cooler months of the year. No age is exempt, but children suffer from the disease in much larger proportion than adults. The greatest susceptibility is between the ages of one and ten years. Males and females are about equally affected. Chronic catarrhal diseases of the nose and throat and hypertrophy of the tonsils seem to increase the liability to infection. Persons suffering from scarlatina, measles or pertussis are especially susceptible to diphtheria. Overcrowding and defective ventilation of necessity favor the propagation of the disease, but good hygienic surroundings do not insure immunity from its attacks.

Diphtheria is highly contagious. While it is often transmitted directly by patients with typical lesions of the disease, it is more frequently spread by convalescents in whose bucco-nasal secretions bacilli are still present, by individuals suffering from mild and unrecognized forms of diphtheria or by healthy persons (carriers) who have been in contact with the sick and who harbor the infective organisms in their throats, but who have sufficient resistance to prevent the development of the disease in themselves.

[1] Amer. Jour. Med. Sci., April, 1920.

The usual mode of conveyance is by immediate contact, as in kissing, or by contact transference through the agency of mouth spray containing the bacilli or of fingers soiled with infective secretions. Indirect transmission by means of contaminated handkerchiefs, toys, pencils, etc., of dust impregnated with dried mucus from a patient's throat, or of milk infected by healthy carriers may also occur, but is uncommon. It seems to have been definitely established that diphtheria is occasionally transmitted by domestic animals, especially cats, (Low, Karlinski, Simmons.)[1] An attack of diphtheria produces only a temporary immunity.

**Bacteriology.**—The *Bacillus diphtheriæ* was discovered by Klebs in 1883, and first cultivated by Loeffler in 1884. It is a non-motile, non-spore bearing, straight or slightly curved rod, somewhat shorter and thicker than the tubercle bacillus, and, in films made from the false membrane, frequently club-shaped at the ends. It varies, however, both in shape and size with the medium upon which it is grown. When stained with Loeffler's methylene blue it presents a beaded, granular or striated appearance which is somewhat characteristic. The organism grows best on Loeffler's blood serum mixture. On this medium colonies appear in from twelve to twenty-four hours as small white or grayish-white dots. The culture is most luxuriant when the temperature is maintained at about 37° C. (99° F.) and oxygen is freely admitted. Other organisms commonly found in the throat are much slower in growth. The medium at first becomes acid and later alkaline in reaction.

The diphtheria bacillus is resistant to desiccation and may retain its vitality in dry membrane for several months.

*Pathogenesis.*—Klebs-Loeffler bacilli from different sources vary widely in their ability to produce toxins, some strains being extremely virulent, while others are apparently harmless. Animal experimentation is the only means of determining the pathogenicity of the organism. When 0.5 c.c. fresh bouillon culture is injected subcutaneously in the median abdominal line an inflammatory edema occurs at the site of inoculation, toxemia develops and the animal dies usually in from 48 to 72 hours. Occasionally death is delayed and then paralysis of the extremities, partial or complete, makes its appearance. Postmortem examination reveals in addition to the local lesions a characteristic hyperemic and hemorrhagic condition of the adrenals.

The local lesions of diphtheria, which clinically are usually on the mucous membrane of the upper air-passages, the constitutional disturbances of the disease, and the histologic changes which are found after death in the internal organs and sometimes in the peripheral nerves are all produced by a soluble toxin generated by the bacilli at the site of inoculation.

*Distribution.*—As a rule, diphtheria bacilli are found only at or near the primary point of infection in the mucosa. Bacteremia is exceptional, although in fatal cases it is not uncommon to find a few organisms in the blood and internal organs. In 75 per cent. of the cases the infected mucosa is free of bacilli within two weeks after the disappearance of the false membrane, and in 95 per cent. within 4 weeks. Occasionally, however, the organisms persist for much longer periods. Park cites a case in which they were present for six months.

It is important to bear in mind that diphtheria bacilli are sometimes found in cases of acute rhinitis, pharyngitis and tonsillitis when no pseudo-membrane is present and the local appearances are merely those of a simple inflammatory process. Again, it has been shown that genuine diphtheria bacilli are found in the throats of at least 1 or 2 per cent. of all well persons

[1] Amer. Jour. Med. Sci., Oct., 1920.

in urban communities and in the throats of from 8 to 50 per cent. of all persons who have been recently exposed to diphtheria.

*Pseudodiphtheria Bacilli.*—Organisms are not rarely found in non-diphtheritic sore throats, and also in the upper air-passages, urinary tract, and conjunctiva of well persons, which do not differ morphologically from true diphtheria bacilli, but which lack the ability of the latter to produce specific toxins. These have been called pseudo-diphtheria bacilli. As a rule, they do not show typical granules when stained by Neisser's method and do not ferment dextrose, but animal experiment is the only positive means of differentiating them from true diphtheria bacilli. Some authorities regard them as variants of Klebs-Loeffler bacilli which have lost their virulence.

*Mixed Infections.*—As in scarlet fever and smallpox, mixed infections, especially with streptococci, are common in diphtheria and in many of the secondary complications of the disease, such as bronchopneumonia, suppuration of the middle ear, and phlegmonous adenitis, pyogenic cocci play the major rôle.

*Individual Susceptibility.*—Susceptibility to diphtheria varies considerably in different individuals and in the same individual at different ages.

Relatively few infants in the first year of life are attacked. Schick[1] in 1913 devised a simple clinical test which makes it possible to differentiate susceptible from non-susceptible persons. The action depends on the local irritant effects of minute quantities of diphtheria toxin when injected intracutaneously in individuals who possess no immunity. In applying the test the requisite amount of toxin ($\frac{1}{50}$ of the minimum dose of toxin lethal for a guinea pig and contained in 0.1 to 0.2 mil of normal saline solution) is injected *into the skin*, just beneath the epidermis, by means of an accurately gauged syringe and a long fine needle. By injecting the toxin intracutaneously it remains in the dense tissue sufficiently long to exert its irritant action. If the reaction is positive a red area, usually from $\frac{1}{2}$ to 2 cm., develops about the injection point in from 24 to 48 hours, becomes very pronounced at the end of the third or fourth day, and then gradually fades, the skin later becoming brownish and scaly. If the reaction is negative, as it proves to be in persons who are immune to diphtheria, no erythema occurs about the site of the injection. Pseudo-reactions also signify immunity. They appear within the first 12 to 24 hours, are less sharply defined than true reactions, disappear in 36 to 72 hours, and leave no pigmentation. Results with the test show that from 40 to 50 per cent. of normal children from 1 to 15 years of age and from 80 to 90 per cent. of adults are naturally immune to diphtheria. Schick's test is particularly useful in determining the susceptibles among children in institutions and among individuals generally who are likely to come in contact with diphtheria patients.

**Morbid Anatomy.**—The characteristic lesion is the *false membrane*, which in the vast majority of cases is found on some part of the upper respiratory tract. In a clinical study of 1962 cases Burrows[2] states that both tonsils were affected in 1528; one tonsil in 243; uvula in 404; postpharyngeal wall in 173; palate in 244; nose in 71; larynx in 337; lips in 12; tongue in 3; inner surface of the cheek in 1; auditory canal in 1; conjunctiva in 1; vulva in 1; and a denuded area of the skin in 1. In 127 fatal cases examined by Councilman, Mallory and Pearce[3] a definite membrane was present on the tonsils in 65; epiglottis, in 60; larynx, in 75; trachea, in 66; pharynx, in 51;

[1] Münch. med. Woch., 1913, lx, 2608.
[2] Amer. Jour. Med. Sci., Feb., 1901.
[3] Bacteriology and Pathology of Diphtheria, 1901.

nose, in 43; bronchi, in 42; soft palate, including uvula, in 13; esophagus, in 12; tongue, in 9; stomach, in 5; duodenum, in 1; vagina, in 2; vulva, in 1; skin of ear, in 1; and conjunctiva, in 1.

The membrane is usually of a whitish, yellowish, or dirty-gray color, but occasionally it is almost black. In the throat it is for the most part adherent to the underlying tissue, and when removed leaves a raw surface. In the larynx and trachea it is often easily detached. According to Councilman, Mallory and Pearce, the process by which the membranous formation is effected is as follows: First the epithelial cells undergo degeneration and necrosis, either breaking up into detritus, or becoming changed into refractive hyaline masses. Subsequently, an inflammatory exudation rich in fibrin ferment issues from the underlying tissue, and fibrin is formed when this comes in contact with the necrotic epithelium. The fibrin in part is formed into a reticulum around exudation, cells and degenerated epithelium; in part it combines with the hyaline degenerated cells to form a hyaline membrane. The membrane never develops primarily on an intact epithelial surface, but it may extend over it. The underlying tissues are the seat of changes which represent a combination of degeneration and exudation.

It must be borne in mind that diphtheric infection may exist in the entire absence of false membrane, the process being manifested locally by catarrhal inflammation or, more rarely, by a gangrenous lesion.

Besides the local changes, other lesions due to the absorption of the toxins produced by the diphtheria bacilli or to the entrance of other organisms are invariably present. The *lymph-nodes* in the neighborhood of the infection atrium are enlarged and show circumscribed or diffuse necrosis and extensive cellular infiltration. *Bronchopneumonia* is present in a large proportion of cases and is often the immediate cause of death. Examination of the *heart muscle* reveals distention of the small vessels, minute blood extravasations, cloudy swelling and fatty degeneration of the muscle fibers, and not rarely interstitial myocarditis with focal accumulation of leucocytes. Tanaka, Liebman[1] and others have described an eosinophilous myocarditis in diphtheria. The *kidneys* may show no changes other than cloudy swelling, but in severe cases they may present the changes of acute interstitial nephritis. The *adrenals* are often enlarged and intensely congested. In the *liver* the important changes are cloudy swelling and fatty degeneration of the cells, disseminated foci of necrosis, and proliferation of the endothelial cells of the capillaries. The *spleen* may or may not be swollen, but microscopically it usually shows minute areas of necrosis, and evidences of endothelial proliferation. In some cases degenerative changes are found in various *peripheral nerves*, especially those which supply the pharynx and muscles of the eye.

**Symptoms.**—The *period of incubation* is usually from 2 to 3 days, but it may be as short as 24 hours or as long as a week. The symptoms vary considerably according to the location of the membrane and the severity of the infection.

*Faucial Diphtheria.*—In many cases the disease begins with chilliness, lassitude, anorexia, headache, muscular soreness, and nausea or vomiting. In other cases the first complaint is of soreness in the throat, slight stiffness of the neck, and painful deglutition. Upon examination, the tonsils, palate, uvula, and posterior pharyngeal wall are found to be reddened and more or less swollen. In the course of a few hours small patches of *pseudomembrane* appear on some parts of the inflamed surface, usually on one or both tonsils or the uvula. Except in the mildest cases the patches tend to spread rapidly and, if multiple, to coalesce, so that in some instances all the visible parts of

[1] Deutsch. Arch. f. klin. Med., 1915, 17, 438.

the throat are covered in from 36 to 48 hours. From the throat the membranous formation may spread in various directions. Sometimes it extends to the nares and thence to the lachrymal ducts or the Eustachian tubes. In other cases it spreads to the larynx and trachea and even to the bronchi. Less frequently it extends to the esophagus. Exceptionally, the structures anterior to the pharynx, such as the mouth, tongue, gums and lips are also invaded.

The membrane is usually of a yellowish-white or grayish-white color, but in grave cases it may be almost black. It may be thick and opaque or thin and almost transparent. Sometimes it can be removed with ease, but commonly it is intimately adherent and when forcibly detached leaves a raw bleeding surface upon which new membrane forms within a few hours. The affected parts, especially the tonsils and uvula, are often greatly swollen, and in consequence, deglutition, articulation, and even breathing may be rendered difficult. Pain is variable; occasionally there is none at all. A more or less abundant mucous or mucopurulent discharge occurs from the fauces, the tongue is coated, and the breath is often offensive.

The *submaxillary and cervical lymph-nodes* are usually swollen and tender and in virulent forms of the disease all the tissues about them may be so infiltrated that the natural outlines of the neck are obliterated. The severity of the intoxication is not always proportionate to the extent of the local disease. A grave or even fatal toxemia may occur with a very circumscribed throat lesion and on, the other hand, cases are occasionally observed in which the entire pharynx is covered with false membrane and yet the constitutional disturbance is slight. The *temperature* is not characteristic and is rarely high. As a rule, it ranges between 101° and 103° F. In some cases, even severe ones, the temperature is scarcely at any time above the normal. A continued high fever is suggestive of some complication. The *pulse* is frequent, ranging between 100 to 130 in cases of moderate severity. As the disease advances it becomes small and weak, and not rarely irregular. Bradycardia is usually an indication of heart failure and is of serious import.

The *general condition* of the patient may remain good throughout the attack, but marked pallor and profound muscular weakness frequently occur as a result of the toxemia. Except at the onset, the *stomach* is ordinarily retentive. Persistent vomiting at the height of the disease is of grave significance and is usually a forerunner of heart failure. *Nervous symptoms* are not, as a rule, pronounced, but in severe cases, a typhoid condition with delirium of the muttering type may ensue. The *urine* contains more or less albumin and in a large proportion of cases a few hyaline casts. *Leucocytosis* of the polymorphonuclear type (15,000 to 40,000) is the rule. It may be absent, however, in very mild or very severe cases.

The duration of an attack of diphtheria is variable. Cases of average severity usually last from ten days to two weeks. In very mild attacks the symptoms begin to subside after the third or fourth day and by the seventh day the fauces are clear. Complications often prolong the period of convalescence for weeks or even months.

*Nasal Diphtheria.*—The mucosa of the nose is not infrequently attacked primarily, especially in infants, but in the majority of cases it is involved by extension of the diphtheritic process from the pharynx. There are many cases of nasal diphtheria in which the symptoms are those of ordinary coryza and bacteriologic examination is the only means of determining the specific nature of the inflammation. As a rule, however, the clinical picture is characteristic. The discharge is profuse and acrid and produces excoriations at the edges of the nostrils and on the upper lip. Sometimes it is very

offensive. Bleeding is likely to occur and may prove refractory. The lymph-nodes about the angles of the jaw soon become swollen and tender. As the nostrils are either partially or wholly occluded by the tumefaction and false membrane, mouth breathing is made necessary. Not rarely false membrane is seen on inspecting the nares or later is found as a cast in the discharge. Owing to the rich supply of lymphatics to the nasopharynx, the constitutional disturbance is generally more severe than in faucial diphtheria. In exceptional cases the pseudomembranous inflammation may extend along the lachrymal duct and reach the conjunctiva or it may pass through the Eustachian tube and involve the middle ear.

*Membranous or Fibrinous Rhinitis.*—In this curious condition, which has also been called chronic nasal diphtheria, false membrane appears on the mucous membrane of the nose and persists for from 3 to 6 weeks or longer. There is little tendency for the membrane to extend beyond the nasal cavities and the constitutional symptoms are slight. Moreover, in only a few instances has the disease occurred in more than one member of a family. Clinically, therefore, membranous rhinitis is unlike diphtheria, but in most cases diphtheria bacilli are present in the secretions. According to Ravenel[1] Klebs-Loeffler bacilli were found in 33 of 41 cases examined bacteriologically. Nearly all the cases on record have been in children.

*Laryngeal Diphtheria (Pseudomembranous Croup or True Croup.*—The larynx is usually affected by the downward extension of pharyngeal diphtheria, but cases are sometimes observed in which the pseudomembranous inflammation begins in the larynx. According to Burrows,[2] the larynx was involved in 337 (18 per cent.) of the 1962 cases of diphtheria observed by him in the Boston City Hospital during the years 1899 and 1900. Slight hoarseness of the voice and a harsh dry metallic cough are usually the first symptoms of the laryngeal involvement. A little later signs of stenosis appear. These increase in intensity, although for a time there may be intervals, especially during the day, in which the patient is comparatively or, perhaps, entirely comfortable. The dyspneic attacks are peculiar in that both inspiration and expiration are prolonged and labored. Occasionally the difficulty in breathing is accompanied by a whistling or wheezing stridor, which may be audible at a considerable distance. As the obstruction increases, the voice gradually sinks to a whisper, the cough grows husky and feeble, and the dyspnea becomes more severe and continuous. When the obstruction is marked the child is restless, tosses about in bed, throws back its head, opens its mouth, dilates its nostrils, and often clutches at near-by objects or at its own throat in the vain effort to obtain air. All the accessory muscles of respiration are brought into action and with each inspiration there is retraction of the lower part of the thorax with sinking in of the soft parts above the clavicles. The face is anxious, the lips are livid, and the skin is covered with clammy sweat. Unless the condition is relieved by the expulsion of the membrane or by operative intervention, asphyxia speedily ensues, the mind becoming dull, the pulse frequent and feeble, the respiration more and more shallow and the surface cold and blue. Finally, drowsiness supervenes and gradually deepens into coma. The fever and other signs of systemic poisoning are usually much less pronounced when the involvement is laryngeal than when it is faucial.

The course of laryngeal diphtheria is somewhat variable. Cases with little impediment to respiration often respond promptly to medical treatment and end favorably with a fewin days without operation. On the other hand,

[1] Medical News, May 18, 1895.
[2] Amer. Jour. Med. Sci., Feb., 1901.

cases in which the signs of laryngeal stenosis are marked may terminate fatally within forty-eight hours. Suffocation is often averted and life saved, however, by prompt recourse to intubation or tracheotomy. Despite these measures death sometimes results from the extension of the membrane into the bronchi. Occasionally all urgent symptoms are suddenly relieved by a violent paroxysm of coughing and the expectoration of large fragments of membrane. When this occurs there is still danger of a fatal issue, for new membrane may form in the larynx or the inflammation may spread to the finer bronchi and set up bronchopneumonia. As a rule, when recovery occurs spontaneously, without operation, the membrane undergoes molecular disintegration or liquefaction and the symptoms subside gradually. Hoarseness of the voice and croupy cough not infrequently remain for a week or more after the dyspnea has abated.

*Septic Diphtheria.*—The local and constitutional symptoms of diphtheria are often rendered especially severe by secondary infection of the tissues with pyogenic cocci. In these septic cases both the nose and throat are usually affected. The membrane is extensive and frequently of a dark gray or brownish color. It is soft and tends to separate here and there in shreds. The breath is horribly offensive. Large quantities of viscid phlegm collect in the throat, impeding respiration and increasing the difficulty of deglutition. The lymph-nodes at the angles of the jaw and the surrounding cellular tissue rapidly swell, and sometimes the tumefaction is excessive. Suppuration and even sloughing may supervene. An erythematous rash, such as frequently occurs in other septic processes, not rarely appears on the skin. The temperature is high, the pulse frequent, and the prostration profound. A fatal termination is the rule, and when recovery does occur it is only after a long struggle extending over many weeks.

*Malignant Diphtheria.*—In this form the system is so overwhelmed by the specific toxin that death occurs in from 24 to 72 hours. The face is pale and swollen; the temperature is not high and may be subnormal; the pulse early becomes extremely small and feeble; hemorrhages not rarely occur from the mucous membranes and into the skin; the mind may be clear until near the end, but as a rule, somnolence or stupor supervene with great rapidity.

*Latent Diphtheria.*—As stated elsewhere diphtheria is not invariably accompanied by membranous exudation. There are cases in which the disease takes the form of simple coryza or sore throat or of follicular tonsillitis with absolutely nothing in the local appearances to betray the specific nature of the inflammation. Without a bacteriologic examination of the secretions the recognition of these latent forms of the disease is only possible when the patient infects another person with manifest diphtheria or peculiar paralytic symptoms supervene.

**Complications.**—*Bronchopneumonia* is a frequent cause of death. It is especially common in laryngeal diphtheria. The disease is usually due to secondary infection with pneumococci or pyogenic bacteria, although diphtheria bacilli themselves seem capable of exciting it. Lobar pneumonia is rare.

*Heart failure* is common, and while it usually occurs at the end of the second or the beginning of the third week, during convalescence, it may show itself at any period of the disease. It has been variously ascribed to degenerative changes in the myocardium, in the bundle of His, or in the cardiac ganglia or nerve fibers in the heart, to failure of the vasomotor control of the arteries (Romberg and Pässler, MacCallum), and to exhaustion of the suprarenal glands (Ritchie and Bruce). The usual signs of heart failure are pallor of the face, coldness of the extremities, irregular action of the heart, a feeble

and greatly accelerated pulse, and soft systolic murmur at the apex with accentuation of the pulmonic second sound. The area of heart dulness may or may not be increased. In very grave cases the cardiac disturbance is ushered in with epigastric pain and tenderness, vomiting, extreme prostration, and gallop rhythm. Progressive enlargement of the liver may also occur and is of ill omen (Rolleston). Less commonly there is bradycardia, the pulse dropping quickly from 120 or thereabouts to 40 or even 30 per minute. Fatal syncope without premonitory symptoms is rare. Endocarditis was found in only 7 of the 220 cases examined post-mortem by Councilman, Mallory and Pearce.[1]

*Diphtheritic Paralysis.*—Besides the cardiac disturbances already mentioned, which in some instances may be due to changes in the nerves of the heart, paralysis in various parts of the body occurs in from 10 to 20 per cent. of all cases of diphtheria, the frequency of the complication varying in different epidemics. The lesion responsible for the paralysis is apparently a toxic neuritis, which involves especially the motor fibers of the nerve. In the majority of cases the symptoms develop during convalescence, in the third or fourth week after the onset of the diphtheria (postdiphtheritic paralysis), but they may appear while the local lesions are still present. According to Rolleston[2] it is exceptional for paralysis to occur after the sixth week. While palsy may follow the mildest attacks of diphtheria it is more likely to occur when the infection is severe. It is uncommon in pure laryngeal diphtheria. In about two-thirds of the cases the paralysis affects solely or chiefly the palate and pharyngeal muscles, the symptoms being a nasal tone of the voice and difficulty in swallowing, sometimes with regurgitation of fluids through the nose. Not rarely the sensibility of the pharynx is also impaired. Occasionally, the interference with deglutition is so pronounced that feeding through an esophageal tube is made imperative. Next to the palatal and pharyngeal muscles those of the eyes are most frequently affected. In 472 cases of diphtheritic palsy observed by Woollacott[3] the eyes were involved in 104. The commonest disturbance is failure of accommodation from paresis of the ciliary muscles, but strabismus from paresis of the extrinsic muscles, especially the external recti, is by no means rare.

The muscles of the extremities sometimes suffer and in such cases the symptoms may be similar to those of ordinary multiple neuritis, except that pain is rarely pronounced. Even when there is no appreciable weakness of the muscles the patellar reflexes may be impaired or abolished. Exceptionally the paralysis affects the larynx, the neck, the face, the diaphragm, or the bladder. Excluding the cases of heart failure, some of which may be due to changes in the cardiac nerves, death occasionally results from paralysis of the respiratory muscles, aspiration pneumonia, or the impaction of a foreign body in the larynx. Generally speaking however, the prognosis is good and complete recovery usually ensues in from a few weeks to several months.

*Cerebral paralysis* (hemiplegia) is an unusual sequel. In 1913 Rolleston[4] collected 80 cases. Degenerative changes in the renal epithelium, shown by a moderate albuminuria and cylindruria, occur in the majority of cases, but *acute nephritis* with suppression of urine, edema or uremia, is uncommon. *Otitis media* developed in 3 per cent. of 1962 cases studied by Burrows[5]

[1] Loc. cit.
[2] Archiv. of Pediatrics, 1913, xxx, 335.
[3] Lancet, Aug. 26, 1899.
[4] Clin. Jour., 1913, xlii, 12.
[5] Loc. cit.

and in 4.1 per cent. of 5076 cases analyzed by Rolleston.[1] The discharge from the meatus may contain diphtheria bacilli as well as pyogenic cocci.

*Destruction* of the *cornea* and *optic neuritis* are rare complications. *Tonsillitis*, due to invasion of the tonsils by various pyogenic bacteria, sometimes occurs during convalescence. Rolleston observed it in 7 per cent. of 900 consecutive cases under his care. A few cases of *gangrene in peripheral parts*, the result of vascular lesions, have been reported. Finally, it is not uncommon for diphtheria to coexist with other *acute specific infections*, especially scarlet fever and measles. As a rule, the one infection develops during the decline of the other.

**Diagnosis.**—The diagnosis of diphtheria is rarely difficult in typical cases. It must be borne in mind, however, that membranous inflammations sometimes occur in the absence of diphtheria. Even membranous laryngitis, or true croup, is exceptionally due to other organisms than the Klebs-Loeffler bacillus. These so-called *diphtheroid inflammations* are usually excited by the streptococcus, but cases are occasionally observed in which the pneumococcus, staphylococcus, bacillus of Friedländer, or Bacillus pyocyaneus is the only organism present. As it is frequently impossible to differentiate such conditions from true diphtheria by either the local appearances or the general symptoms, all cases of membranous pharyngitis, rhinitis or laryngitis should be regarded as diphtheritic until proved otherwise by bacteriologic examination. On the other hand, it must not be forgotten that diphtheria is not always accompanied by the formation of pseudomembrane and may present the same naked-eye appearances as a simple catarrhal inflammation. If there is any doubt as to the nature of the process in a given case it may readily be dispelled by a bacteriologic examination. In *follicular tonsillitis*, which may readily be confused with the milder forms of diphtheria, the onset is, as a rule, more sudden and there is usually no distinct membrane but in its stead a number of yellowish-white deposits, which are confined to the tonsil, which show no special tendency to run together, and which can readily be removed by a swab without leaving a raw surface. However, in many cases the two diseases cannot be positively differentiated without the assistance of the bacteriologist. *Vincent's angina* may closely resemble diphtheria, but the lesions develop more slowly, are usually confined to one tonsil or one side of the throat, and are more definitely ulcerative than those of diphtheria. The diagnosis can be established by finding the characteristic spirilla and fusiform bacilli in smears from the ulcer. It is sometimes difficult at first to distinguish between *spasmodic croup* (catarrhal laryngitis) in a child and laryngeal diphtheria. In the former, however, the obstruction usually comes on abruptly and especially at night; it is paroxysmal throughout; it affects chiefly the respiration; and it yields readily to sedatives and emetics. Moreover, in spasmodic croup the voice is hoarse but not lost, and the cough retains its ringing character. Laryngoscopic examination would, of course, yield conclusive evidence but it is not feasible in young children. Occasionally *syphilitic lesions* of the throat may closely similate diphtheria, but the history of the case, the concomitant symptoms of syphilis, and the results of the bacteriologic examination of the faucial secretions will soon settle the question. The differential diagnosis between *scarlet fever* and diphtheria is considered on p. 224.

**Prognosis.**—The prognosis should always be guarded, since even the mildest cases may become serious through the extension of the diphtheritic process or the occurrence of some complication, such as heart failure

[1] Brit. Jour. Child. Dis., 1915, xii, 18.

or bronchopneumonia. The mortality varies considerably in different epidemics. Before the introduction of antitoxin treatment the average death-rate in all forms of diphtheria was from 30 to 35 per cent. and in membranous croup about 70 per cent. At present the average death-rate in all forms of the disease is from 10 to 15 per cent. and in membranous croup from 30 to 35 per cent. When serum treatment is commenced on the first day of the disease the mortality does not exceed 3 per cent. During nine consecutive years (1904–1913), covering the treatment of 741 such cases in the Philadelphia Hospital for Contagious Diseases, not a single death occurred (Kolmer[1]). Age has an important bearing on the prognosis. More than 50 per cent. of the deaths occur in children under 5 years of age. In individual cases of faucial diphtheria marked glandular swelling, an offensive discharge, profound asthenia, a weak and irregular pulse, and late vomiting are unfavorable features. Bradycardia is always ominous. The danger is not always proportionate to the extent of the membranous formation or the height of the temperature.

Death may be due to exhaustion incident to the general toxemia, sudden heart failure, asphyxia, bronchopneumonia, or paralysis.

**Prophylaxis.**—The important measures are (1) segregation of all infected individuals; (2) exclusion of exposed persons from school and public gatherings until a bacteriologic examination shows that their mucous membranes are free from diphtheria bacilli; (3) immunization of all contacts or of contacts shown by Schick's test to be susceptible to diphtheria; (4) activ-immunization of all children entering hospitals or asylums who yield positive reaction with the Schick test; (5) disinfection of the nasopharyngeal secretions of infected persons and of all articles soiled therewith; (6) thorough cleaning, airing and disinfection of rooms that have been occupied by patients; and (7) search for and appropriate treatment of diphtheria carriers.

The *segregation* of infected persons should be continued until at least two consecutive negative cultures from the nose and throat, taken not less than 24 hours apart, show that diphtheria bacilli are no longer present, or, if bacteriologic assistance is not available, until the false membrane has been absent from the parts that were affected for at least 3 weeks.

As from two to three weeks are required to produce active immunity, persons who have come in intimate contact with a case of diphtheria should be *passively immunized.* This is accomplished by the subcutaneous administration of antitoxin, 500 units[2] for infants under 1 year of age and 1000 units for older children and adults. By this method complete protection is afforded for from 2 to 4 weeks. *Active immunization,* although more slowly developed than passive immunization, is much more persistent and is therefore preferable when time permits. The material employed for the purpose "consists of a mixture of strong diphtheria toxin and antitoxin in such proportions that the toxin is just neutralized or is in very slight excess when tested on a guinea pig." Three injections are given subcutaneously at weekly intervals, the dose being 0.5 mil for infants under one year and 1 mil for older children and adults. According to Park[3] one injection gives immunity to 80 per cent. of those previously susceptible, two injections to 90 per cent. and three injections to 97 per cent. The immunity conferred lasts for at least 3 years and probably much longer. Park has seen no serious untoward effects from the injections in 10,000 cases.

[1] Kolmer: Infection, Immunity, and Specific Therapy, 1917.

[2] A unit is the amount of antitoxin which will just neutralize 100 minimal fatal doses of toxin for a guinea-pig weighing 250 grams.

[3] Archiv. of Pediatrics, May, 1919.

Various methods of ridding *carriers* of the diphtheria bacillus have been tried. Local applications to the nose and throat of silver nitrate solutions (2–10 per cent.), argyrol solutions (25–50 per cent.), Dakin's solution, tincture of iodin, antidiphtheritic serum and emulsions of staphylococcus pyogenes aureus and of lactic acid bacilli have been used with indifferent success. Insufflations of fuller's earth (kaolin), three times a day, after the method of Rappaport and Hektoen[1] have been found satisfactory in adults, but not in children (Rabinoff). Removal of tonsils and adenoids has given the best results and should be resorted to when other measures fail.

**Treatment.**—The sick-room should be well ventilated and the temperature maintained at about 68° F. In laryngeal cases it is desirable to have the atmosphere moist and this may be accomplished by generating steam in a croup-kettle or in an ordinary kettle. Absolute rest must be enforced. Even in mild cases the patient should not leave the bed for at least three weeks and if there have been signs of cardiac failure or of paralysis the period of inactivity should be much longer. The diet should consist of bland, nutritious, liquid or semi-liquid foods. Milk, junket, ice-cream, soft boiled eggs, animal broths, gelatin, and gruels are suitable forms of nourishment. If sufficient nutriment cannot be swallowed recourse must be had to gavage or to rectal feeding. Cool water should be given freely. The bowels should be opened at the beginning of the attack, preferably by calomel, followed by milk of magnesia or citrated magnesia, and kept open throughout the illness by laxatives or the use of enemas.

Statistical reports from all parts of the world during the last 25 years prove conclusively that the one remedy of great value in the treatment of diphtheria is the blood serum of a horse that has been immunized by a series of injections of diphtheria toxin. This serum, or antitoxin, as it is commonly called, neutralizes the toxin of the disease and apparently aids in destroying the bacilli, probably by favoring phagocytosis (Kolmer). It should be used at the earliest moment possible and in suspicious cases at once without waiting for a report of the culture. The dose varies with the location and extent of the lesion, the degree of toxemia, the day of the disease when treatment is begun, and the age of the patient. In cases of faucial or tonsillar diphtheria which are of moderate severity and which are first seen on the second day, the initial dose should not be less than 10,000 units. If the patient is seen on the first day and the patch is small and confined to one tonsil, 5000 units will usually suffice. In laryngeal diphtheria the dose should be from 10,000 to 20,000 units according to the time at which treatment is instituted. In well-marked nasal diphtheria, unless the patient is seen very early, the dose should not be less than 15,000 units. Age need only be considered in the case of young children under 2 years, and in them the dose should be about one-half of that required for older persons. Unless there is a very definite improvement, as shown by the appearance of the throat and the patient's general condition, the treatment should be repeated in twelve hours. In severe cases, if no improvement is observed, a second and larger should be given in six hours. In some cases it is necessary to administer three, four or more doses of antitoxin, and to use in the aggregate from 50,000 to 100,000 units. The danger lies not in using too much, but in using too little.

Except in malignant or profoundly toxic cases, when it may be given intravenously, antitoxin should be injected subcutaneously or intramuscularly, preferably in the pectoral region, abdominal wall, or flank. The injections should be made under aseptic precautions.

Untoward effects sometimes follow the use of serum therapy. *Serum*

[1] Jour. Amer. Med. Assoc., Mar. 25, 1916.

*sickness,* which is characterized by an urticarial or erythematous rash and in some instances by arthralgia, nausea, vomiting, edema, and depression, is not uncommon. *Anaphylactic shock* may also occur, but fortunately it is rare. Most of the fatal cases have been in persons in whom contact with horses has regularly caused asthma, paroxysms of sneezing, or urticaria. The symptoms develop suddenly and consist of intense dyspnea, cyanosis, edema, respiratory failure and collapse. If there is any reason to suspect the possibility of such a reaction, the physician may inject 0.5 mil of antitoxin for the purpose of producing anti-anaphylaxis, and two or three hours later administer the remainder of the requisite dose. If anaphylaxis does occur it should be treated by injections of atropin and morphin and, if necessary, by artificial respiration.

Apart from the use of antitoxin, the internal treatment of diphtheria is entirely symptomatic. Caffein, strychnin, digitalis or camphor are frequently required to combat circulatory failure. To secure rest and relieve distress, morphin, in small doses, is sometimes a very useful adjuvant to cardiac stimulants. Proctoclysis with hot normal salt solution may be of value when collapse seems imminent. Notwithstanding the fact that much has been written against the use of alcohol, many clinicians of large experience believe that this drug is decidedly useful when asthenia is pronounced. For a child of three or four years a dram (4.0 mils) may be given every three or four hours.

*Local Treatment.*—Local treatment is of value in securing cleanliness of the affected parts. It cannot destroy the bacteria. Applications should be made with the utmost gentleness and should be unirritating. If they cause violent struggling and exhaust the child it is better to omit them. Irrigation is preferable to spraying, gargling or swabbing. The nozzle of the irrigator should be blunt and covered with soft rubber, and the nurse should be instructed to introduce it gently in a horizontal direction. In both nasal and pharyngeal diphtheria, if the child cannot be raised, the fluid may be poured into the nose from a spoon or better from a nasal cup (Jacobi). Among the best irrigating fluids are hot (100°–105° F.) normal salt solution, Dobell's solution, diluted three or four times, and boric acid solution (2 per cent.). Externally, hot or cold applications to the throat, whichever may be more grateful to the patient, are sometimes of service. Small pieces of ice held in the mouth tend to relieve soreness and dysphagia. In laryngeal diphtheria when dyspnea becomes marked and recession of the suprasternal and infrasternal regions occurs with each inspiration intubation or tracheotomy is indicated. *Intubation* is usually given the preference, but *tracheotomy* may be required after intubation has been tried and has failed to remove the obstruction, owing to excessive edema of the fauces or to the presence of membrane below the tube.

*Paralysis.*—If the soft palate and pharynx are affected and swallowing becomes difficult or impossible recourse must be had temporarily to gavage. Strychnin, $\frac{1}{100}$ grain (0.0006 gm), three times a day, at 4 years, is useful. In paralysis of the muscles of the neck, shoulders or limbs massage and electricity may also be of service.

*Convalescence* must be managed with special care on account of the tendency to cardiac failure. Anemia, a common sequel, will require a nutritious diet, and the use of tonics, especially iron.

## INFLUENZA

(La Grippe)

**Definition.**—Influenza is a specific, infectious and contagious disease, probably caused by Bacillus influenzæ (Pfeiffer), occurring in pandemic, epidemic, and endemic forms, and characterized by fever, general aching, inflammation of the mucosæ, especially those of the respiratory tract, and marked prostration.

**Epidemiology.**—Our knowledge of the disease dates from the tenth century. Since that time numerous outbreaks have occurred, not a few of which have been world-wide in extent. The first to be recorded in the United States was in the summer of 1655. During the nineteenth century there were four pandemics, 1830–32, 1836, 1847–48, 1889–90. The last world-wide outbreak, that of 1918, like most of its predecessors, seems to have originated in eastern Europe or western Asia. It spread westward along the chief avenues of migration with remarkable rapidity, invading successively the continent of Europe, Great Britain and North America, and attacking millions of persons. Virtually every epidemic has been followed by secondary outbreaks of greater or less severity for a period of two or three years or longer. The usual duration of an epidemic in a given locality is from 4 to 8 weeks.

Influenza is contagious, the infecting microörganism, which is present in droplets of secretion expelled by the patient in coughing and sneezing, producing the disease in a susceptible person when it enters the body by way of the air-passages. Doubtless, as in the case of diphtheria and cerebrospinal fever, healthy carriers of the inciting agent also play an important part in disseminating the infection.

Influenza may prevail at any season. While the majority of epidemics have been in the winter and spring months, some of the most severe outbreaks have occurred in warm weather. Personal predisposition to the disease is very general and when the infection first makes its appearance in a community a large proportion of the population, sometimes more than 50 per cent., are attacked. While no age is exempt, infants and old persons show less disposition to infection than others. The robust are apparently as susceptible as the weak. One attack of the disease seems to afford a certain degree of immunity, but the protection is transient and recurrences are common.

**Etiology.**—The Bacillus influenzæ, described by Pfeiffer in 1892, is generally accepted as the cause of influenza, although in the pandemic of 1918 many competent observers failed to find this organism in a large proportion of cases. Whatever the inciting agent, it is undoubtedly one that breaks down the body defenses and favors the growth of other pathogenic bacteria. Indeed, it is this secondary invasion by microbes commonly present in the nasopharynx, such as pneumococci, streptococci, staphylococci and meningococci, rather than the primary specific infection, which is chiefly responsible for the severe effects and high mortality of the disease in some epidemics.

The Bacillus influenzæ, which is found in the secretions of the nose and throat, in the sputum, in pneumonic exudates, and occasionally in the blood, is a small ($0.2 \times 0.5\mu$) non-motile rod. It forms no spores, is a strong aërobe, and grows readily only on media containing blood. It is best stained with a 10 per cent. aqueous solution of carbolfuchsin and is Gram negative. It shows little resistance to unfavorable conditions, such as drying and extremes of temperature, and even in sputum it rarely survives more than 48 hours.

As Pfeiffer's bacillus is found in the sputum in certain acute and chronic pulmonary conditions and not rarely in the buccal secretions of healthy persons, even when influenza is not prevalent, it must be concluded that some strains of the organism are more virulent than others, or that individual susceptibility varies considerably from time to time, or that Bacillus influenzæ is only a secondary invader and not the specific cause of influenza. It is certain that influenza-like outbreaks are not rarely observed in which Pfeiffer's bacillus plays no part, the inciting agent being a streptococcus, pneumococcus, or micrococcus catarrhalis. The term *pseudo-influenza* has been applied to these outbreaks.

**Morbid Anatomy.**—Influenza in itself is rarely fatal and produces no characteristic changes. Death is almost invariably a result of secondary infection and in the vast majority of cases is immediately due to pneumonia. The latter varies in form according to the nature of the bacteria accompanying Bacillus influenzæ, but it is almost always a bronchopneumonia, with discrete lobular areas of consolidation well scattered through both lungs, or, not rarely, a massive lobar infiltration produced by the confluence of many small bronchopneumonic areas. In fulminating cases there may be no actual consolidation, but merely intense engorgement, with hemorrhagic extravasations and serous effusion into the alveoli. Emphysema, sometimes pronounced, is usually found in portions of the lung that are not solidified. The bronchial lymph-nodes are commonly enlarged. The mucous membrane of the throat, trachea and bronchi is the seat of catarrhal inflammation and the submucous tissues often show minute hemorrhages. Pleurisy with fibrinous, serofibrinous or sero-sanguinofibrinous exudate is a common finding, and cases coming to autopsy in the later days of an epidemic frequently show empyema. Purulent pericarditis may accompany the latter or more rarely occur as an independent condition. In some outbreaks inflammation of the gastrointestinal tract is a fairly common finding. The heart, liver, kidneys and spleen exhibit varying degrees of congestion and of granular degeneration.

**Symptoms.**—The incubation period is short, usually from 1 to 3 days, and the onset is sudden, often extremely abrupt. The symptoms are so varied that they are best grouped into classes.

*Ordinary Form.*—The important features in the majority of cases in most epidemics are chilliness or occasionally, a distinct rigor; fever, which rises quickly to 102° to 104,° runs an irregular course for four or five days, and ends by crisis or rapid lysis; intense aching in the head, eyeballs, back and limbs; catarrh of the upper respiratory tract, with sneezing, hard cough and scanty mucous or mucopurulent expectoration; muscular weakness out of all proportion to the severity of the fever or any existing local inflammation, and pronounced depression of spirits.

In the first few days of the disease the pulse may not be accelerated in proportion to the degree of fever, a rate of 90 or 100 often occurring with a temperature of 104° F. The blood pressure is usually low. In the epidemic of 1918 nosebleed was somewhat common and occasionally there were hemorrhages from other organs, especially the uterus or the stomach. A striking symptom in many of the severe cases is peculiar cyanosis of the lips, ears and fingers, sometimes extending over the entire body. This cyanosis is not a result of circulatory failure or respiratory embarrassment, but is probably of toxic origin and due to changes in the blood itself. Nausea and vomiting not rarely occur at the onset and occasionally prove refractory to treatment. At the height of severe attacks there may be slight delirium, especially at night. Herpes is frequent in some outbreaks and compara-

tively rare in others. The spleen may or may not be enlarged. In the absence of complications, examination of the blood almost always shows a leukopenia. Albumin and casts are often found in the urine and exceptionally there are evidences of acute hemorrhagic nephritis.

Convalescence is, as a rule, rapid, although in some instances it is very tardy and marked by subnormal temperature, anorexia, general weakness, paroxysmal cough, neuralgic pains, and persistent mental depression.

*Respiratory Form.*—In this form, which was the prevalent one in the epidemic of 1918, catarrh of the respiratory tract is the dominant feature. Cough is present from the onset or develops in the course of two or three days. At first it is dry, but later it is accompanied by more or less mucopurulent or thin salmon-colored or reddish expectoration. The temperature is usually between 102° and 104° F. Pain in the region of the sternum or on one or both sides of the chest is common. Profuse sweating also occurs in many of the cases. The physical signs are variable and subject to marked changes from day to day. In mild cases with bronchitis as the only intrathoracic lesion general weakness of the respiratory murmur with a greater or less number of loud musical or coarse mucous râles is the usual finding. Significant of developing bronchopneumonia, which is an extremely common complication, are hyporesonance, feebleness or suppression of the breath sounds, and fine crackling râles over certain areas of the lungs, most frequently in the lower lobes.

Not rarely the râles become apparent only upon deep breathing or coughing. With the coalescence of the bronchopneumonic patches the percussion dulness becomes more pronounced and bronchovesicular or bronchial breathing often replaces the feeble respiratory murmur. Even when bronchial breathing does not develop, the voice sounds usually become exaggerated and the râles often acquire a peculiar sharp metallic quality. Pleurisy with effusion may or may not accompany the pneumonia. In the latter part of the epidemic of 1918 it was common. With the occurrence of pneumonia a moderate leucocytosis usually develops and the rate of the breathing is increased, although there is often little embarrassment of the respiration even when the lungs are extensively infiltrated. The mind may remain clear throughout, but frequently delirium, usually muttering, but occasionally active, supervenes. When the catarrhal process is confined to the upper respiratory tract, the symptoms usually subside in from a few days to a week. Occasionally, however, the cough persists for weeks or months. Pneumonia may develop at any stage of the disease, even in the first twenty-four hours, or it may occur several days after the temperature has reached normal, especially if the patient has gotten about too soon. It always makes the outlook very serious, but not hopeless. Recovery often ensues and is usually complete. On the other hand, a certain amount of consolidation sometimes remains in the lung and in this event the patient may lapse into a condition closely resembling pulmonary tuberculosis both in its general symptoms and physical signs.

*Gastro-intestinal Form.*—In this form, which was not uncommon in the epidemic of 1889, but comparatively rare in that of 1918, the infection expresses itself locally as an acute gastroenteritis, thus producing in addition to the usual constitutional symptoms of the disease, abdominal pain, nausea, vomiting and diarrhea. In some cases the symptoms resemble those of cholera morbus, while in others they are suggestive of dysentery. The duration of the attack is usually from 3 to 4 days, but it may be much longer.

*Nervous Form.*—In this type of influenza, which was more frequently observed in 1889 than in 1918, the catarrhal symptoms are often slight or entirely wanting, the chief features, apart from the febrile disturbance, being profound prostration, insomnia, psychic depression, and intense pain in the head and back and about the joints. Delirium, occasionally more or less maniacal, is not uncommon. Nervous complications, especially peripheral neuritis, are more likely to develop in this than in other forms of the disease.

*Fulminant Form.*—In this comparatively rare form of influenza, the onset is abrupt with a chill, the temperature is high, the toxemia is profound, and the local symptoms and signs are those of acute pulmonary edema. Death occurs before pneumonia has had time to develop, usually in from 24 to 48 hours.

*Other Forms.*—In every epidemic many cases occur in which the symptoms are so mild that they are usually ascribed to an ordinary cold. Doubtless these ambulatory cases play an important part in disseminating the infection. Occasionally attacks of influenza are observed which simulate more or less closely typhoid fever. Moderate fever extending over a period of two or three weeks may be the only conspicuous symptom, or with persistent pyrexia there may be somnolence, mild delirium, a dry, brown, glazed tongue, tympanites and a tendency to diarrhea. In rare instances the heart seems to bear the brunt of the attack, the important features being an extremely weak, frequent, and perhaps, irregular pulse, precordial pain, dyspnea and a tendency to syncope.

**Complications and Sequels.**—In many epidemics complications are common and varied. *Pneumonia* is especially important, as it is the usual cause of death. In the outbreak of 1918 it occurred in from 20 to 25 per cent. of the well marked cases. Like other lesions of influenza it is usually a result of secondary infection, although in rare instances it is apparently due to Pfeiffer's bacillus alone. Persistence of the consolidation is more frequently observed than in ordinary pneumonia. That *chronic bronchitis* and *bronchiectasis* may be dependent upon chronic infection with the influenza bacillus has been clearly demonstrated by a number of writers (Leichtenstern, Lord, Boggs and others). The clinical resemblance of chronic influenza (unresolved pneumonia and bronchiectasis) to pulmonary tuberculosis is sometimes very close and the differential diagnosis between the two conditions is made more difficult by the fact that old, quiescent tuberculosis is not rarely made active by influenza. *Pleurisy* and *empyema*, localized or diffuse, are somewhat common, especially in the later stages of an epidemic. *Inflammation of the nasal accessory sinuses* and of the *middle ear* are not infrequent. *Anosmia* sometimes persists in consequence of olfactory neuritis.

*Pericarditis* occasionally develops. *Endocarditis* is rare. *Myocarditis* is sometimes observed and *disturbances of the nervous mechanism of the heart* are not uncommon. *Cardiac pain* of an anginoid character is also an occasional sequel, but it is usually transient. *Arterial thrombosis*, although a very rare complication seems to be more frequent in influenza than in most of the infections. Of 166 instances of this lesion collected by Eichhorst[1] 19 were due to influenza. *Acute nephritis* occurs in small proportion of cases. *Pyelonephritis*, *perinephric abscess*, *cystitis*, *epididymo-orchitis* are exceptional complications.

A number of nervous affections are met with as sequels of influenza. Of these *peripheral neuritis* and *persistent asthenia* are apparently the most

[1] Deutsch. Arch. f. klin. Med., 1901, lxx.

common. Gross lesions of the central nervous system, are less frequent, but *meningitis, encephalitis* and *myelitis* have been observed. In 1911 Wollstein[1] collected 49 cases of influenzal meningitis and in 1916 Torrey[2] collected 28 additional cases. The disease has occurred chiefly in young children. *Postinfluenzal psychoses* are not very rare. Confusional insanity is the most common mental disturbance. Unless there is a special predisposition to insanity, the prognosis as to complete recovery is good. The duration of the disorder varies from a few weeks to a few months.

**Relapse.**—A return of the symptoms after an afebrile period of a few days is fairly common. While the relapse may equal or exceed in severity the primary attack it is usually milder and of shorter duration. Persistent secondary febrile disturbances are always suggestive of bronchopneumonia or pleurisy.

**Diagnosis.**—Typical cases are readily recognized, especially during an epidemic. The diagnosis of atypical cases is often difficult. Important points are the sudden onset, the high temperature with a relatively slow pulse, prostration out of all proportion to the coexisting symptoms and signs, the frequent presence of catarrhal phenomena, and leucopenia. The nervous form of influenza may sometimes be difficult to distinguish from *cerebrospinal meningitis* without recourse to lumbar puncture. *Typhoid fever* is occasionally confused with influenza, but, as a rule, the less sudden onset, the gradual rise of temperature, the roseolar rash and the positive Widal reaction will lead to a correct diagnosis. Chronic influenzal pneumonia may closely simulate *pulmonary tuberculosis*. However, if the signs of consolidation are confined to the base of the chest, if there is a clear history of an acute febrile attack at the onset, and if tubercle bacilli are persistently absent from the sputum a strong suspicion of influenza should be entertained. In the comparatively rare cases of chronic apical influenza the bacteriologic tests are the only criteria.

**Prognosis.**—Influenza very rarely proves fatal except through complications. The mortality varies in different epidemics, but whenever the disease is widespread in a community, the death-rate, especially from respiratory conditions, is usually enormously increased. In Philadelphia during seven weeks of the epidemic of 1918 more than 12,000 deaths were reported from influenza and pneumonia, whereas the number of deaths from the latter disease during the corresponding period of 1917 was less than 300. In 1217 cases of influenza treated at the Naval Hospital, Philadelphia, in 1918[3] the total death-rate, irrespective of complications, was 11.6 per cent. Doubtless the average mortality of the cases occurring in the civil population was much less, as many of the patients in the Naval Hospital were admitted to the institution at a late period of their infection. In the epidemic of 1889 the disease was of a distinctly milder character, but reliable mortality statistics are not available.

In individual cases of influenza, cyanosis, severe nervous disturbances, especially meningism, bloody expectoration, and signs and symptoms of pneumonia are of serious import. Various estimates place the mortality of influenzal pneumonia at from 20 to 50 per cent. The disease is exceedingly fatal in pregnant women and usually results in premature labor or abortion. In the analysis of 89 cases of influenzal meningitis made by Torrey[4] the death-rate was 91 per cent.

[1] Amer. Jour. Dis. of Children, 1911, i, 42.
[2] Amer. Jour. Med. Sci., clii, No. 3.
[3] U. S. Naval Med. Bull., 1919, vol. 13, No. 4.
[4] *Loc. cit.*

**Prophylaxis.**—The most efficacious measures are segregation of the sick so far as this is feasible; collection of the sputum in special containers and its disinfection; the use of correctly constructed gauze masks by physicians, nurses, attendants and others who come in intimate contact with the sick; the prohibition of public gatherings; and the education of the public in regard to the danger of contact with persons presenting catarrhal symptoms. Quarantine is of doubtful utility, and this is true also of vaccination with mixtures of bacteria isolated in influenza.

**Treatment.**—The most important features of the treatment are immediate and complete rest in bed, an abundance of fresh air without draft, a liberal diet of easily digestible food, and attentive, skillful nursing. Owing to the possibility of relapse and complications, especially pneumonia, the rest should be maintained for at least a week after the fever and other symptoms have entirely disappeared. The bowels should be moved freely at the onset preferably by calomel and a saline, and should be kept open throughout the attack. Water should be given in abundance.

In mild cases a hot foot-bath and the administration every three hours of an alkaline diuretic, such as the official solution of potassium citrate (4 drams— 15.0 mils), and of a moderate dose of Dover's powder (5 grains— 0.3 gm.) at night, for two or three nights, will suffice. For the relief of pains in the head, back and limbs moderate doses of acetylsalicylic acid or of acetphenetidin are useful. Although some prejudice exists against these drugs, they promote comfort and very rarely do harm, unless given in large doses or for long periods. A combination such as the following is often satisfactory:

℞. Codeinæ sulphatis..... gr. ii (0.016 gm.)
Acetphenetidini
Acidi acetylsalicylici.....āā gr. xl (2.5 gm.)
Pone in capsulas No. xii M.
Sig.—One every three hours.

Or,

℞. Acetphenetidini..... gr. xl (2.5 gm.)
Sodii benzoatis..... ʒi (4.0 gm.)
Fiant chartulæ No. xii. M.
Sig.—One every three hours.

As a rule, analgesics of this class should not be continued beyond the second day. Excessive cough is best controlled by codein in full doses or morphin (1/6 grain— 0.01 gm.) and the application of sinapisms or of dry cups to the chest. Spasmodic cough is sometimes favorably influenced by impregnating the air of the room with steam from a croup kettle which contains a dram or two (4.0–8.0 mils) of compound tincture of benzoin or eucalyptol, or 30 minims (2.0 mils) of creosote to each quart of water.

With the first appreciable evidence of circulatory weakness, it is advisable to give digitalis by the mouth or intramuscularly. If the toxemia is profound, caffein in doses of from 1 to 2 grains (0.06–0.13 gm.), three or four times a day, may be used as an adjuvant to digitalis. Proctoclysis with normal salt solution or a 5 per cent. solution of glucose is sometimes helpful.

In threatened collapse with signs of pulmonary edema intramuscular injections of camphor should be tried. From 1 to 2 grains (0.065–0.13 gm.) of the drug in oil may be given every two or three hours. Atropin (1/100 grain— 0.0006 gm.), repeated two or three times at intervals of two hours, may also be given. For pronounced insomnia bromides or veronal, may be tried, but, usually, morphin is the only satisfactory remedy.

Convalescence should be carefully guarded. After severe attacks the

patient should abstain from undue activity for two or three weeks or longer. Tonics are usually indicated. Change of air and scene materially help in restoring strength and overcoming the peculiar mental depression.

## CHOLERA

(Asiatic Cholera)

**Definition.**—Cholera is an acute, specific infectious disease, chiefly epidemic, but endemic in the lowlands of India, characterized by diarrheal discharges of a so-called rice-water character, painful cramps of the muscles, and a marked tendency to collapse.

The disease is said to have been known in India from early antiquity, but the first epidemic of which there is an accurate record began in the delta of the Ganges in 1817 and during the next six years spread westward over the greater part of Asia and eastward to the confines of Africa and Europe. Since 1817 numerous other epidemics have occurred in India and eight or nine times the infection has spread thence to Europe. In the United States there have been five important outbreaks (1832–36, 1848–49, 1853–54, 1866–67, 1873).

**Etiology.**—The exciting cause of cholera is the *Spirillum choleræ*, first recognized by Koch in 1883. This organism, which may be found in the stools in every case of cholera, is a comma-shaped rod from 1 to 2 microns long and 0.4 microns thick, with a single flagellum at one end. It is motile, non-spore forming, grows readily in various culture media of an alkaline reaction, produces indol, stains with the usual anilin dyes and is Gram-negative.

*Vitality.*—The cholera spirillum has comparatively little resistance to injurious influences. In ordinary drinking water it does not remain alive for more than a week. In milk and on the surface of fruits and vegetables it dies within a few days. In human dejecta it may retain its vitality from 2 to 7 days. It is rapidly destroyed by drying, sunlight, boiling water, and comparatively weak solutions of chemical disinfectants.

*Pathogenicity and Immunity.*—The poison responsible for the symptom-complex of cholera is probably in large part an intracellular substance, or endotoxin, which is set free upon the disintegration of the bacterium, and in small part a true soluble toxin (Metchnikoff, Roux, Kraus). Animals may readily be immunized against infection by inoculation first with killed cultures and later with increasing doses of living organisms. Cholera spirilla are very quickly agglutinated by the blood serum of immunized animals even when it is diluted many thousand times. Further, when injected into the peritoneum of an immunized animal, the bacilli do not increase, but undergo disintegration (Pfeiffer's reaction). By these phenomena it is possible to distinguish with certainty true cholera spirilla from other spirilla having similar morphologic and cultural characteristics.

*Mode of Infection.*—Cholera is directly transmissible from man to man. So far as is known the alimentary tract is the only infection atrium. The normal gastric juice, on account of its acidity, and the healthy intestinal mucosa afford a certain amount of protection against infection. For this reason, and others less obvious, a certain proportion of individuals who ingest the organisms do not become infected. Once having gained access to the bowel of a susceptible person, however, the spirilla penetrate the mucous

membrane and cause desquamation of epithelium and intense irritation. At the same time the specific poisons liberated from the spirilla enter the blood and give rise to an acute intoxication.

Cholera spirilla are found in large numbers in the rice-water stools, but not often in the internal organs; nevertheless, Greig[1] found them in patches of bronchopneumonia, in the spleen and in the bile, and believes that chronic cholera carriers, like typhoid carriers, owe their prolonged infections to the persistence of the inciting organisms in the gall-bladder. While spirilla are sometimes found in the stools of convalescents and healthy carriers for periods of one or even two months, they do not usually persist longer than one or two weeks.

Cholera is frequently spread by personal contact, and in many outbreaks persons with mild and unrecognized forms of the disease and carriers are the chief sources of infection. In the case of nurses, attendants and laundry women there is a distinct danger, unless scrupulous care is exercised, of the organisms being transferred from the discharges of the patient, either directly or indirectly, by the fingers. Large explosive epidemics of the disease, such as that which occurred in Hamburg in 1892, in which 17,000 persons of a population of 600,000 were attacked, are usually due to contamination of the water-supply with the stools of cholera patients or of cholera carriers. Shellfish, milk, celery, lettuce, and other articles of food that are commonly used in an uncooked state are sometimes the vehicles by which cholera bacilli are transferred to the alimentary canal. In the epidemic which occurred in Madeira in 1911 and in that which occurred in Manila in 1914 the infection was disseminated almost entirely by personal contact with convalescents or carriers or by food handled by such persons, and in each instance it was finally stamped out by the rigid segregation of all "contacts." Occasionally the contamination of food by flies which have been in contact with cholera dejecta has been an important factor in the spread of the disease. In a few instances cholera has been acquired in the laboratory through the accidental ingestion of cultures of the specific germ.

*Epidemics.*—Cholera is disseminated by human intercourse. Starting from its home in India it has invariably advanced along the lines of commerce or pilgrimage. Owing to increased facilities of travel and intercommunication it may now be carried as far in a few months as it was formerly in several years. Once having gained a foothold in a community its spread is favored by insanitary conditions. In general its progress is arrested in winter and resumed in the warmer months of the year. In individuals alcoholic intemperance, exhaustion, and digestive disturbances increase the susceptibility to infection. Permanent immunity is not acquired by one attack.

**Morbid Anatomy.**—The body is shrunken and livid. Rigor mortis is marked and persistent. The subcutaneous tissue is remarkably dry. The right ventricle of the heart is filled with thick, dark blood; the left ventricle is empty. The serous membranes are sticky and lusterless, and often present petechial extravasations. The lungs are usually dry and pale, but sometimes they are congested and edematous, and occasionally they show patches of bronchopneumonia. The kidneys, although almost normal in their macroscopic appearance, always exhibit microscopically a more or less intense parenchymatous degeneration, the tubules in severe cases being distended with fatty and necrotic epithelium. The bladder is, as a rule, found empty, the anuria which is often an important feature of the disease being due to dehydration, subnormal bloodpressure, renal stasis and, in many cases, an acute nephrosis. The liver is of normal size or slightly contracted, dry, and,

[1] Indian Jour. Med. Research, 1914, i, 67.

not rarely, of a dark red color. Evidences of cholecystitis are sometimes present. The spleen is not enlarged.

The intestinal changes are the most constant. The contents of the bowel consist of a grayish-white, turbid fluid, in which are suspended small clumps of detached epithelium and flakes of mucus ("rice-water" material). The spirilla are found not only in the liquid contents, but also in and beneath the epithelial lining of the bowel. The mucosa, especially of the ileum, is sodden, of a pinkish color, and often studded with hemorrhagic spots. Exfoliation of the superficial epithelium is everywhere apparent. The lymph follicles, both solitary and agminated, are enlarged and prominent. Occasionally, deposits of pseudomembrane are seen.

**Symptoms.**—In accordance with general custom four stages of the disease may be recognized, if it be understood that these stages merge insensibly one into the other and are not all developed in every case.

*Invasion.*—After a period of incubation lasting from a few hours to four or five days, symptoms of acute intestinal catarrh set in. These consist of frequent loose stools, flatulence, colicky pains, epigastric discomfort, and anorexia. In many cases headache, malaise, and depression of spirits are also noted. Slight fever may or may not be present. This stage is of short duration; indeed, it is often entirely absent, the disease beginning abruptly and almost at once attaining its full intensity.

*Stage of Evacuation.*—The essential features of this stage are violent purging, vomiting, and muscular cramps. The stools are frequent, very copious and watery. They soon loose their feculent character and acquire the appearance of thin gruel or of water in which rice has been boiled, the white particles being flakes of mucus and epithelium. Occasionally a small quantity of blood is discharged. Colic is often present, but is rarely severe. In the majority of cases the diarrhea is accompanied by persistent vomiting. The vomitus, which is usually expelled with much force, consists first of undigested food and later of material closely resembling the rice-water stools.

The muscular cramps, which are intensely painful, begin in the extremitus, especially in the calves of the legs and in the thighs, and later extend to the muscles of the arms, hands, feet, and trunk. To add to the distress there is intense thirst and sometimes hiccough. Signs of depression make their appearance and soon culminate in collapse. The duration of this stage is from two to twelve hours, rarely longer.

*Stage of Collapse.*—This stage, which is also known as the algid stage is, marked by almost complete arrest of the circulation. The eyes are sunken, the cheeks are hollow, the nose is sharp, the skin is wrinkled and inelastic, and the surface is more or less livid, cold and covered with clammy sweat. The breath is cool and the voice is feeble or quite extinct. The respirations are labored and shallow; the pulse is extremely weak, the systolic blood-pressure sometimes falling to 60 or even to 50. The temperature in the axilla is subnormal, often below 95° F., while in the rectum it may be 102° or 103° F., or higher. The urinary secretion is totally suppressed. The evacuations and cramps may continue, although the former often cease when the depression of vitality becomes very profound. The mind while apathetic, is usually clear, except toward the close in fatal cases, when stupor or coma is likely to supervene. This stage lasts from a few hours to one or two days, and generally ends in death, but sometimes, even when the condition seems utterly hopeless, a gradual restoration of the suspended functions may occur.

*Stage of Reaction.*—The pulse improves, the lividity disappears, the sur-

face temperature rises to its normal or slightly above it; vomiting and purging cease, the stools acquire a bile-stained appearance; urine is again secreted, although for a time it is very turbid and contains albumin and casts; the muscular strength gradually returns, and complete recovery may ensue in from one to two weeks.

The stage of reaction, however, is by no means free from danger. Hyperpyrexia, with a rectal temperature of 106° F. or even 107° or 108° F., sometimes supervenes, and not infrequently the patient lapses into a typhoid state, with moderate fever, dry tongue, muttering delirium, subsultus tendinum, stupor and perhaps coma. This condition, which is generally fatal, has been ascribed to uremia, but it is probably due, in some instances at least, to secondary infection. In other cases the reaction is imperfect or an actual relapse occurs. In either event death is likely to ensue sooner or later from exhaustion, although recovery is not impossible.

Sometimes during the period of reaction an eruption of an erythematous or urticarial character makes its appearance, especially on the extremities, but it is without special significance.

**Varieties.**—In every epidemic there are many cases in which the symptoms do not pass beyond the initial stage. To these mild attacks the term *cholerine* has been applied. On the other hand, fulminant cases are met with in which there is neither vomiting nor purging (*cholera sicca*), the patient being stricken with fatal collapse while at work or during a meal. Between these extremes every gradation exists.

**Complications and Sequelæ.**—*Anuria*, *hyperpyrexia* and the *typhoid state*, to which reference has been made, are the most common complications. Accompanying anuria there is usually pronounced *acidosis*. *Bronchopneumonia*, *parotitis* and certain *ophthalmic lesions*, such as conjunctivitis, keratitis, and iritis, occur somewhat frequently. *Gangrene* of peripheral parts has not rarely been reported. In pregnant women *abortion or premature labor* is almost inevitable. After prolonged attacks there may be persistent malnutrition with anemia, digestive disturbances and a tendency to diarrhea.

**Diagnosis.**—*Cholera morbus*, certain forms of *food poisoning*, and certain *metallic poisonings*, notably antimonial and arsenical, and severe attacks of *bacillary dysentery* may produce symptoms almost identical with those of Asiatic cholera. In doubtful cases bacteriologic studies afford the only means of arriving at a positive diagnosis. In true cholera the discharges contain the specific spirilla and the blood serum possesses agglutinating properties. To distinguish with certainty cholera spirilla from cholera-like organisms it may be necessary to employ not only the usual cultural tests, but also Pfeiffer's reaction.

**Prognosis.**—The death-rate varies with the character and the stage of the epidemic. It is almost invariably highest at the commencement of an outbreak. The mortality averages about 50 per cent. Cholera is extremely dangerous to old persons, young children, and all who are weakened by want, fatigue, alcoholism or chronic disease. In individual cases early collapse, marked cyanosis, persistent anuria, hyperpyrexia, and the typhoid state are features of grave import.

**Prophylaxis.**—General prophylactic measures include the establishment of a judicious quarantine system; the careful protection of the water-supply; the isolation of the sick in screened rooms and the thorough disinfection of their vomitus and stools and of all articles that have been contaminated by their excreta; recognition of carriers and their segregation until they are shown to be free from infection by bacteriologic examination; rigid supervision of overcrowded districts; and the dissemination of information concerning the

nature of the disease and the precautions to be observed in order to escape it. Statistics indicate that vaccination with living cholera bacilli, as practised by Haffkine in India, in 1895, or preferably with heat-killed cultures, after the method of Kolle,[1] confers a certain degree of immunity, although apparently it does lessen materially the case mortality. Two or three doses (first 0.5 mil and then 1.0 mil) of a preparation containing 8000 million organisms per mil usually afford protection for at least three months.

Personal measures of prevention consist in the avoidance of uncooked food, and the restriction of the diet to bland, easily digestible articles; in using no water for drinking or brushing the teeth that has not been previously boiled; in thoroughly cleansing the hands before each meal; in the avoidance of overfatigue, undue excitement, and exposure to cold and wet; and in the prompt treatment of any gastro-intestinal disturbance, however slight, that may arise.

**Treatment.**—From the first appearance of diarrhea the patient should be put to bed and warmly covered. Hot stupes may be applied to the abdomen. Food, other than barley water or whey, which should be given freely, is better avoided. The use of cathartics, even of calomel in fractional doses, is inadvisable, and this is probably true also of opium in any form, although some authorities believe that in the first stage, if there is much discomfort, morphin may be given hypodermically in small doses without risk. There is no specific treatment. Anticholera serum has been used, but without success. Rogers speaks favorably of atropin and potassium permanganate. The former is given hypodermically, morning and evening, in doses of $\frac{1}{100}$ grain (0.0006 gm.), and the latter by the mouth, in pills made up with kaolin and petrolatum, and preferably coated with salol or keratin, the dose being 2 pills, each containing 2 grains (0.13 gm.) of the permanganate, every quarter of an hour for two to four hours, in accordance with the severity of the case, and then two every half hour until the stools change to green or yellow and become comparatively small.

Collapse is best combated by intravenous injections of normal salt solution every few hours, the fluid being introduced slowly until a full pulse has returned. The amount of fluid usually required for each injection is from 1 to 2 quarts (500–1000 mils). The temperature of the fluid should be about 98° F., or lower, if the patient's rectal temperature is high. Proctoclysis is much less effective, but it is useful in supplementing the intravenous injections. Other measures useful in collapse include applications of hot blankets and hot water bottles and the administration intramuscularly of caffein—sodium benzoate, camphor, and pituitary extract. Rogers[2] who has had a large experience in the treatment of cholera, states that hypertonic salt solution is much superior to normal solution in the stage of collapse when the blood pressure is not over 70 mm. and the specific gravity of the blood is 1.063 or over. He uses a solution containing 120 grains (8.0 gm.) of sodium chlorid and 4 grains (0.4 gm.) of calcium chlorid to the pint (500 mils), and injects 3, 4, 5, or even 6 pints, according as the specific gravity of the blood is 1.063, 1.064, 1.065, or 1.066 in male adults and correspondingly less in females and children. Unless the rectal temperature is below 99° F. the solution should never be injected at above blood heat for fear of producing hyperpyrexia, and if the rectal temperature is 100° F. or over the fluid should be given at a temperature between 80° and 90° F. He further advises that normal salt solution should also be given by the rectum, half a pint (250.0 mils), every two hours, until the collapse stage is passed

[1] Deutsch. Med. Woch., 1897, xxiii, 4.
[2] Indian Med. Gaz., 1916, No. I.

and urine is being secreted regularly, and then every four hours until 2 pints of urine are passed in the 24 hours.

In suppression of urine the most promising measures are dry cupping over the kidneys and intravenous and rectal injections of salt solution or, as the anuria is always accompanied by acidosis, intravenous and rectal injections of a 2 per cent. solution of sodium bicarbonate. Sellards has found the alkaline solution just as efficacious in relieving collapse as the salt solution. To allay thirst cracked ice or iced Seltzer water may be given at frequent intervals. The painful cramps are best treated by warm applications or gentle friction with anodyne liniments. In hyperpyrexia cold sponging and rectal injections of cold water should be tried. Antipyretic drugs should be avoided.

In the stage of reaction liquid foods in small quantities are permissible. Milk with lime-water, whey, thin gruels, albumin-water and light broths are the most appropriate. The return to ordinary foods should be effected very gradually. Water should be given freely, since it tends to restore vascular fulness and favors diuresis. Any tendency to recurrent diarrhea should be met by the administration of bismuth subnitrate or bismuth subsalicylate. Bitter tonics are often of service during convalescence. Change of air is a valuable aid to the restoration of health.

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## BACILLARY DYSENTERY

**Definition.**—Bacillary dysentery[1] is an infectious disease, due to Bacillus dysenteriæ, and characterized by intestinal colic, tenesmus, diarrhea with mucosanguinolent stools, and usually more or less toxemia.

**Etiology.**—Bacillus dysenteriæ, which was first described by Shiga in 1898, is an organism similar in appearance to the colon bacillus, but non-motile.

Several types of this bacillus, differing in certain biochemical properties, are now recognized, the most important being the Shiga-Kruse type, the Flexner type, the Y type of Hiss and Russel, and the type of Strong. Of these, the Shiga-Kruse type seems to be the most widely distributed and probably contributes to the highest mortality. In the United States the Flexner type has been the one most frequently encountered.

The Shiga bacilli yield an endotoxin and a soluble exotoxin. In rabbits the former attacks the bowel and the latter the central nervous system. The Flexner bacilli yield only an endotoxin (Flexner). The infection, as in the case of cholera, is confined to the intestines, but the toxic products of the specific bacteria enter the blood and later are excreted into the bowel (Flexner and Sweet).[2]

The sole source of infection in bacillary dysentery is the feces of dysenteric patients, of persons affected with mild or unrecognized forms of the disease, or of healthy or convalescent carriers. The manner of transmission is by the direct transference of infected fecal matter by the hands

[1] The term dysentery is applied to a number of affections characterized anatomically by inflammation of the intestines, especially of the colon, and manifested clinically by abdominal pain, tenesmus, and frequent intestinal discharges containing mucus and blood. The inflammation may be caused by chemical irritants, various bacteria, certain protozoa (Entamœba histolytica, Balantidium coli) or one of the parasitic worms (Bilharzia hæmatobia). Two specific forms of dysentery are especially important, the *bacillary* and the *amebic*.

[2] Jour, Exp., Med., 1906, viii, 514.

to the mouth or by the ingestion of food or water contaminated by infected hands, by direct contact with infected human excreta, or by flies that have had access to dysenteric stools. The specific organisms are sensitive to external influences and do not live long outside of the body; hence explosive epidemics of dysentery due to contamination of the public water supply are rarely observed. Convalescents do not remain carriers for more than a month and chronic healthy carriers do not play an important part in the spread of the disease. In this respect bacillary dysentery differs from both amebic dysentery and typhoid fever.

Bacillary dysentery is especially prevalent in India, Java, the Philippines and other tropical countries, but it frequently occurs elsewhere, both sporadically and in epidemics. In the temperate zone it appears chiefly during the summer and autumn. Overcrowding and unsanitary conditions in general favor its spread, hence it has prevailed extensively at times in military camps, jails, asylums, etc. In the American Civil War there were upward of 300,000 cases in the Federal Army, and in the Franco-Prussian War there were 38,652 cases with 2,830 deaths, equal to one-sixth of all the deaths from disease.[1] Lowered vitality from any cause is a predisposing factor, and in consequence bacillary dysentery is not an uncommon secondary or terminal event in many wasting diseases. The summer diarrheas of children are often due to infection with *B. dysenteriæ*, but in these cases the disease does not often extend with epidemic severity.

**Morbid Anatomy.**—The colon is chiefly affected, but sometimes the lower portion of the ileum is also involved. In the beginning the lesions are those of a follicular catarrh. The mucous membrane is congested and edematous, the lymph-follicles are enlarged and foci of hemorrhage are often present in the mucosa and submucosa. Very soon the mucous membrane forming the crests of the folds undergoes coagulation necrosis, the dead tissue, together with a fibrinous exudate, forming an opaque false membrane. If the infection is severe, the so-called diphtheritic process rapidly spreads from the folds to surrounding parts, and eventually large areas of the bowel are affected. With the separation of the necrotic tissue, irregular denuded surfaces are left, which later are transformed into ulcers. In contrast to the deep undermined ulcers of amebic dysentery, those of the bacillary variety are, as a rule, comparatively superficial and very rarely lead to perforation.

The bacilli may be isolated from the intestinal lesions and swollen mesenteric glands, but only exceptionally from the circulating blood. In some cases Entamœba histolytica is found associated with Bacillus dysenteriæ. In the absence of secondary infection, the viscera do not show pronounced cloudy swelling. Death, when it occurs, is due to poisoning by the toxins of the bacilli and not, as in amebic dysentery, to the local effects of the infection.

**Symptoms.**—After an incubation period of from two to five days, the disease begins somewhat suddenly with colicky pains and diarrhea. In a short time, usually within 24 hours, tenesmus supervenes and the stools become mucous and bloody. When the tenesmus is marked there is an almost constant desire to evacuate the bowels, but the evacuations afford little relief. Occasionally the straining is so intense that it leads to prolapse of the bowel. The stools are small, very offensive, and vary in number from ten to thirty or more in a day. In severe cases they sometimes contain pus and shreds of false membrane, and occasionally in very grave forms of the disease the characteristic small mucous stools are soon replaced by copious watery evacuations, made turbid by particles of clotted blood ("meat-water" stools). The temperature ranges usually between 100° and 103° F.,

[1] *Lehrbuch der Militärhygiene:* Bischoff, Hoffmann and Schwiening, 1912.

the tongue is coated, the appetite is lost, the abdomen is distended and often tender along the course of the colon, and the urine is scanty and deeply colored. Vomiting is not common, but it may occur. Toxic symptoms—muscular pains, headache, muttering delirium, and stupor—frequently occur in severe infections. Weakness and emaciation sometimes appear very rapidly. The blood serum, after eight to ten days, agglutinates dysentery bacilli of the type isolated from the stools. There is usually no leucocytosis.

**Course and Prognosis.**—In fatal cases death occurs usually after 2 or 3 weeks, but it may occur within three or four days. In favorable cases the duration is from a few days to three or four weeks. Occasionally the disease loses its acute character and continues with remissions and exacerbations for an indefinite period. The prognosis depends upon the type of bacillus present, upon the severity of the infection, and upon the previous health of the patient. The range of mortality is from 5 to 40 per cent., the average being about 15 per cent. General speaking, the highest mortality occurs in infection with the Shiga-Kruse bacillus.

**Complications.**—Peritonitis, usually circumscribed and due to extension of the inflammation through the bowel, peripheral neuritis and arthritis are not uncommon. Parotitis, probably the result of secondary infection, occasionally occurs. In certain localities the association of bacillary dysentery with the amebic form is somewhat frequently observed.

**Diagnosis.**—The diagnosis of acute dysentery is usually apparent from the clinical manifestations, but that a given case is of bacillary origin can be definitely determined only by the positive agglutination reactions of the dysenteric bacillus with the blood serum of the patient or by the isolation of the specific bacillus from the feces. In armies it is advisable to regard all outbreaks of diarrhea as dysenteric until proved by bacteriologic tests to be otherwise. In *amebic dysentery* the course is usually chronic, tenesmus is often absent, the specific amebæ are found in the stools, unless there are complications, symptoms of toxemia are rarely observed, and abscess of the liver is of frequent occurrence. *Bilharzial dysentery* may be recognized by the discovery of the characteristic lateral-spined ova in the stools and the occurrence of eosinophilia. Among conditions other than dysentery that must be excluded in the more chronic forms are *carcinoma, syphilis, tuberculosis, and polypi of the rectum, sprue,* and *chronic metallic poisoning.* Fulminant cases of bacillary dysentery closely simulate *cholera.*

**Treatment.**—The prophylactic measures recommended in cholera and typhoid fever are applicable in bacillary dysentery. Vaccines containing several varieties of dysentery bacilli, and prepared from agar or peptone-water cultures, without heat, have been shown to confer a certain degree of immunity, but they often produce severe reactions. Antitoxic serums have also yielded fairly good results in the prophylaxis of dysentery caused by the Shiga type of bacillus, but not of the form due to the Flexner or Hiss type of organism.

In the treatment of acute cases absolute rest in bed is imperative. The diet should consist of milk diluted with barley-water, peptonized milk, infant foods, egg albumin, chicken broth and milk toast. In the more chronic cases soft boiled eggs, pulled bread, steamed rice, oysters, tender meats, wine, jelly and custard may be allowed. An unirritating purgative (magnesium sulphate, castor oil or calomel) is indicated at the onset. After the free purgation, opium should be given to lessen the colic and tenesmus. It may be administered hypodermically in the form of morphin, or by the stomach or bowel. Turpentine stupes or sinapisms over the abdomen are useful. Tenesmus may also be relieved by ice suppositories,

injections of warm mucilage of starch (1 ounce—30.0 mils) or of cocain solution (10 min.—0.6—mils of a 4 per cent. solution) or irrigations with normal saline solution. In the subacute and chronic forms irrigations with solutions of silver nitrate (5 grains gradually increased to 20 grains to the pint—0.3—1.3 gm.—to 500 mils) are sometimes efficacious. These should be given once a day, the fluid being introduced very slowly by means of a fountain syringe with the patient in the dorsal position and with the hips well elevated. Internally, bismuth subcarbonate, 30 grains (2.0 gm.) every three hours, with a dose of castor oil or salts every fourth day, is often efficacious. Antitoxic serums seem to have been of service in some outbreaks. If the exact type of infection is not known a polyvalent serum should be used. As the standard of strength of the different preparations varies, the physician must be guided in the matter of dosage by the printed directions accompanying the package. The average dose for an adult is 20 mils, repeated in from twelve to twenty-four hours if necessary. In severe cases from 50 to 100 mils may be given intravenously. For collapse stimulants and subcutaneous or intravenous injections of saline solution may be used. In chronic cases change of climate is a valuable aid, and sometimes does more for the patient than all other therapeutic measures.

## PYOGENIC INFECTIONS

**(Septicemia; Pyemia; Septicopyemia)**

**Definition.**—The pyogenic infections comprise a group of local or general non-specific infections caused by the entrance and growth within the body of the different pus-producing micro-organisms.

A general intoxication resulting from the absorption of bacterial products formed only at the local source of infection is known as a *toxemia*. The symptoms of this condition differ widely in character with the different bacteria and vary in severity according to the amount of virulence of the toxins absorbed. In the case of the ordinary pyogenic infections removal of the toxin-producing focus is usually followed by recovery. The group of symptoms associated with a general invasion of the blood and tissues by pathogenic bacteria, pyogenic or non-pyogenic, is referred to as a *septicemia*, although formerly this term was applied only to general infections caused by the pyogenic organisms. Removal of the primary focus of infection is much less likely to bring about recovery in a septicemia than it is in a toxemia. However, it is now generally recognized that in many so-called toxemias the organisms themselves enter the general blood-stream in considerable numbers, but the bactericidal action of the blood and tissues is sufficiently powerful to keep them within bounds and to prevent general infection. If in the course of an overwhelming invasion of the blood and tissues by pyogenic bacteria multiple secondary foci of suppuration occur, the condition is described as *pyemia* or *septicopyemia*. These secondary or metastatic foci include abscesses, septic infarcts, ulcerative endocarditis, purulent synovitis, empyema, etc. Obviously, pyemia cannot exist without both septicemia and toxemia. Even in mild septicemias a secondary localization of bacteria with inflammatory reaction frequently occurs in one part or another, although no metastatic foci of suppuration are produced. Thus, a small focus of infection in a tonsil, without pronounced constitutional symptoms, may give rise to a non-suppurative arthritis, endocarditis or nephritis. To infections of

this class the term pyemia is not applicable. From what has been said it is evident that the conditions known respectively as toxemia, septicemia pyemia are but stages of a single process and cannot be separated from one another by any sharp lines of distinction.

**Etiology.**—The bacteria chiefly concerned in the pyogenic infections are Streptococcus hæmolyticus, Streptococcus viridans, Staphylococcus pyogenes aureus, and Staphylococcus albus, but other organisms capable of producing suppuration, such as the pneumococcus, gonococcus, meningococcus, colon bacillus, Friedländer's pneumobacillus, Bacillus pyocyaneus, and Micrococcus tetragenus, may be the offenders. Mixed infections are common.

The chief portals of entry are (1) the *skin*, invasion being effected through wounds or abrasions, (2) the *uterus*, especially after delivery or abortion (puerperal septicemia), (3) the *upper air-passages*, the pharynx and tonsils being often the seat of infection, and (4) the *urethra* (gonorrheal septicemia). Not rarely the most serious general infections originate from a local lesion that is inconspicuous or apparently insignificant, such as a boil, a panaritium, a carious tooth, an infected Fallopian tube, otitis media, a suppurating bronchial lymph-node, or a small tuberculous cavity in the lung. In some instances no local source of infection can be found, either during life or after death, and to this group of cases the term *cryptogenetic septicemia* has been applied.

While wounds, abrasions, contusions, etc., favor the occurrence of local suppuration, the susceptibilityto general infection is much enhanced by overwork, starvation, persistent chilling and other causes that lower the resistance of the tissues. Previous disease is especially potent in this way, as is shown by the great frequency with which pyogenic infections occur as a secondary or terminal event in the course of many chronic diseases of the kidneys, liver, heart, etc. (*terminal infections*). In many of the specific general infections, such as typhoid fever, scarlet fever, and smallpox, there is a septicemia that is due not alone to the organism causing the primary condition, but to some secondary invader, such as the streptococcus or staphylococcus. Even in chronic pulmonary tuberculosis the fatal outcome is usually due to an intercurrent infection rather than to the tubercle bacillus itself.

Organisms of the streptococcus group enter the body through various portals, and once having gained a foothold tend to spread profusely through the tissue, producing extensive inflammatory reactions. Hemolytic streptococci, or streptococci which grow in long chains and produce active hemolysis in blood agar, are the causative agents, as a rule, in puerperal septicemia, diffuse peritonitis and erysipelas. They are also responsible for many of the severe infections originating in open wounds or in the mucous membrane of the throat. Non-hemolytic streptococci, or streptococci producing a green discoloration in blood agar but no hemolysis, are the common cause of chronic septic infections. Staphylococci most frequently enter the body through wounds or abrasions in the skin. They are the causative agents, as a rule, in boils, carbuncles, acute osteomyelitis, and the general infections marked by numerous foci of suppuration.

**Morbid Anatomy.**—The lesions of a septicemia do not differ from those of toxemia, except perhaps in degree. In the more severe general infections small hemorrhagic extravasations are frequently observed beneath the skin and the serous membranes, as well as within the substance of the various organs. The spleen is usually more or less swollen, softened and congested. The lungs are congested and often present areas of pneumonic consolidation. The heart, liver, and kidneys are the seat of cloudy swelling or fatty trans-

formation. In some cases the heart presents evidence of a true interstitial myocarditis. Endocarditis is common, especially in general septicemia due to the staphylococcus, gonococcus or non-hemolytic streptococcus S. viridans. In addition to cloudy swelling or fatty changes, the kidneys may show exudative lesions, multiple foci of necrosis, and hyaline occlusions of the capillaries of the glomeruli. In the liver there may also be numerous minute areas of necrosis. Inflammation of the serous membranes, especially of the pleura and pericardium, is found in many cases.

In pyemia all the changes occurring in toxemia and septicemia are present and in addition secondary foci of suppuration, usually of embolic origin, are found in the lungs or in the territory of the general circulation. When the primary focus of infection is in a part drained by the portal vein metastatic abscesses, with or without suppurative pylephlebitis, occur in the liver.

**Symptoms.**—The local features vary widely, of course, according to the nature and site of the lesion that has served to introduce the infection and also according to the nature and site of any secondary or metastatic processes that may be present. Thus, so far as the local symptoms are concerned, the picture produced by suppuration of the middle ear with extension of the infection to the temporal bone, lateral venous sinus and jugular vein is entirely different from that of tonsillitis with secondary infiltration of the peritonsillar tissues, and the occurrence successively of endocarditis, nephritis and cerebral embolism, or from that of gonorrhea with secondary arthritis and ulcerative endocarditis. In case the infection has occurred through a wound of the skin the discharging pus may change in character, the surrounding tissues may become intensively swollen, red lines may appear on the surface marking the spread of the infection along the lymphatic channels, and the regional lymph-nodes may become swollen and tender. In puerperal infection the lochia often becomes extremely foul.

The constitutional symptoms vary with the character and severity of the infection, and those of toxemia differ from those of septicemia only in degree. Mild cases are usually characterized by chilliness, fever reaching 101° or 102° F., headache, muscular pains, anorexia, a hot dry skin, and restlessness. These symptoms subside rapidly, as a rule, after appropriate local treatment. In severe attacks the onset is marked by a distinct chill and a sudden rise of temperature to 104° F. or higher. Chills, followed by sweating, occur at intervals and the temperature continues high with pronounced daily remissions or even with intermissions. The usual concomitants of fever are present, there is vomiting, sometimes with diarrhea, and the patient becomes weak and rapidly emaciates. The mind may remain clear, but in many cases there is early delirium. Petechiæ in the skin and erythematous rashes, sometimes with pin-point hemorrhages, are not uncommon, especially in streptococcus infections. Owing to extensive destruction of the red corpuscles, profound anemia often supervenes. Occasionally there is slight jaundice. Except in the mildest and in the severest cases, well-marked polymorphonuclear leucocytosis (15,000–30,000) is the rule in all acute pyogenic infections. In many cases of septicemia the bacteria concerned in the infection can be demonstrated in cultures from the circulating blood. The urine is concentrated, often albuminous, and may contain hyaline and granular casts. As the disease progresses a state of collapse may ensue and lead to a fatal termination within a few days, or a typhoidal condition may develop and continue for several weeks. Pyemia presents all the phenomena of severe septicemia and, in addition, the symptoms arising from secondary or metastatic foci of suppuration in the lungs, liver, kidney, lymph-nodes, etc. Death occurs usually in from one to three weeks.

In infections with streptococci of the viridans group the course is often chronic, lasting for weeks or months, and for long periods the disease may be marked only by irregular fever, an occasional chill, and increasing pallor and weakness. Exacerbations, however, occur more or less frequently. Cases with lesions of the heart valves (see p. 675) may readily be misinterpreted unless careful search is made for local signs. Petechial rashes, which are common, are helpful in the diagnosis. Leucocytosis is often absent.

**Diagnosis.**—The diagnosis of septicemia is easy, as a rule, when the disease occurs in connection with an open wound, with an abscess, or with parturition. It is based upon the occurrence of irregular fever with chills, sweating, leucocytosis, pallor and emaciation. In the absence of any evident portal of infection, however, the diagnosis is often very difficult, especially in the more chronic cases, in which there is sometimes little or no leucocytosis and for a long period fever and progressive weakness are the only conspicuous symptoms. In such cases bacteriologic examinations of the blood may be very helpful, although negative results, which are by no means uncommon, leave the diagnosis still doubtful. Cases of subacute infective endocarditis, which is really a pyemic manifestation, of prostatic abscess, of acute osteomyelitis, and of suppuration of the bronchial and other deep lymph-nodes often fail of recognition.

Among common diseases, typhoid fever, malaria, and acute miliary tuberculosis are the ones most likely to be confused with septicemia. *Typhoid fever* may usually be differentiated by the steadiness of the fever, the presence of the rose-colored rash and agglutination reaction, the absence of leucocytosis and the isolation of typhoid bacilli from the blood; *malaria*, by the discovery of the specific parasites in the blood, the low leucocyte count and the therapeutic test; and *acute miliary tuberculosis*, by the evidence of local tuberculosis in the lungs, joints, lumph-nodes, choroid, or elsewhere, the demonstration of tubercle bacilli in the sputum or spinal fluid, the diffuse cyanosis, and the occurrence of leucopenia or of moderate leucocytosis with an excess of lymphocytes. Other conditions which may cause long-continued fever and which, therefore, may be mistaken for septicemia are cholelithias is with a ball-valve calculus in the common bile-duct, lymphosarcoma or tuberculosis of the mediastinal, retroperitoneal or other deep lymph-nodes, rapidly growing carcinoma, visceral syphilis, Hodgkin's disease, and profound anemia.

Blood cultures are the only means of determining with certainty the type of the bacteriemia that is causing the infection.

**Prognosis.**—The prognosis depends upon the type and severity of the infection, the possibility of removing the infectious foci, and the resistance of the patient. Contrary to the belief formerly held, true septicemia (bacteriemia), even if due to the streptococcus, is not necessarily hopeless; indeed the milder forms with local lesions that can be reached surgically often end in recovery. On the whole, however, septicemia is a dangerous malady, and pyemia accompanied by ulcerative endocarditis, meningitis, suppurative pylephlebitis, or multiple visceral abscesses is almost invariably fatal. The duration varies from a few days or weeks in the acute forms to many months in the so-called chronic cases.

**Treatment.**—The chief indications are to evacuate and drain all suppurative foci that are accessible and to conserve the strength of the patient by good hygienic conditions, careful nursing, and a liberal supply of nutritious, easily assimilable food. Water should be used freely. If it cannot be taken by the mouth in sufficient quantity, it should be given in the form of normal saline solution by rectal, subcutaneous or intravenous injection.

Alcohol in moderate amounts is undoubtedly of value. Quinin in tonic doses is apparently of service. Strychnin and digitalis may be required to ward off threatened collapse. The fever is best controlled by cold sponging. Coal-tar antipyretics should not be employed. Morphin may have to be given for pain or insomnia.

Intravenous injections of Credé's colloid silver, of formaldehyd, or other antiseptics have not yielded encouraging results. In acute streptococcus infections antistreptococcus serum, if properly administered, is harmless and sometimes seems to be efficacious, especially if used early and in large doses. To obtain the best results the serum should be polyvalent and should be given intravenously or intramuscularly. In severe cases from 50 to 100 mils should be given at once and repeated in from 12 to 24 hours. In streptococcus endocarditis, the results, on the whole, have been unfavorable. Regarding staphylococcus infections, no satisfactory serum has yet been prepared. In acute septicemia vaccines are rarely beneficial, but in the more chronic infections, they may be of considerable value in conjunction with appropriate surgical treatment. Stock vaccines may be used, although autogenous vaccines are likely to yield better results.

## TERMINAL INFECTIONS

In many chronic wasting diseases, such as chronic nephritis, cirrhosis of the liver, arteriosclerosis, myocarditis, leukemia, etc., the immediate cause of death is some secondary or so-called terminal infection, the occurrence of which has been favored by the lowered resistance of the tissues. The infective agent is usually the streptococcus, staphylococcus, or pneumococcus, but it may be B. tuberculosis, B. coli, B. pyocyaneus, or B. proteus. The infection, which is often cryptogenetic, may be general, without any gross lesions in the organs, or it may be local. The latter is by far the more common, the localization usually taking the form of pneumonia, pyococcic or tuberculous infection of one of the serous membranes (pleura, pericardium, or peritoneum), endocarditis, ileocolitis or meningitis. The symptoms may be those of a frank septicemia with or without distinctive local features, but in many cases the process is entirely latent, fever and progressive weakness being the only indications.

## FOCAL INFECTION

It is now generally recognized that a chronic focus of infection, even though it is inconspicuous and apparently trivial, may be the dominant etiologic factor in producing any one of a large group of systemic diseases, most of which develop insidiously and progress slowly. The faucial tonsils and the teeth and their adnexa are the most common primary seats of confined septic infection, but the accessory nasal sinuses, middle ear, seminal vesicles, prostate gland, Fallopian tube, gallbladder and appendix are other structures that must frequently be considered. As regards the tonsil, a history of repeated attacks of sore throat, a congested appearance of the surrounding tissues, and the discovery of infective material in the crypts will often suggest the source of the metastasis. The size of the gland is also important, but it needs to be emphasized that a small, "submerged" fibrous tonsil is as frequently associated with systemic disease as the conspicuous hypertrophied tonsil. In the mouth the conditions most favorable to the development of metastatic infection are alveolar abscess and pyorrhea. The alveolar abscess being a closed process is especially dangerous. Inspection alone may reveal the condition, but in the large majority of cases

roentgenographic studies are indispensable. Crowns and bridge-work should always excite suspicion.

The organisms most frequently responsible for focal infection are Streptococcus hæmolyticus, Streptococcus viridans, Staphylococcus aureus or albus, the pneumococcus, and colon bacillus. Tonsillitis and septic lesions of the teeth and gums are probably the chief sources of infection by Streptococcus viridans. The local focus of infection is to be regarded not only as a portal of entry, but also as a site in which the organisms multiply, develop their virulent properties, and, perhaps, as Rosenow has suggested, acquire a specific pathogenicity and an elective affinity for certain tissues. Once the defensive powers of the tissues have been overcome, systemic invasion from a primary infected focus may be by way of the blood or lymph stream. Hematogenous infection, however, is the rule. The reaction in the part secondarily invaded may result in a sero-fibrinous or purulent exudate, proliferative changes or necrosis according to the peculiar susceptibility of the tissues and the number, character and virulence of the parasitic invaders. Aggravation of the systemic disease often occurs coincidently with exacerbations of the focal process. It must be borne in mind, however, that the most obvious focus of infection is not always the source from which invasion actually occurs and, moreover, that metastatic lesions once thoroughly established may serve to perpetuate a systemic infection, even after the spontaneous disappearance or surgical removal of the original focus.

Of the conditions that may result from local infection arthritis, endocarditis, and nephritis are the most common, but it seems clear that in certain cases myositis, neuritis, so-called idiopathic osteomyelitis, chronic myocardial disease with various functional disturbances of the heart, and subacute and chronic non-tuberculous infections of the lungs have a similar origin. There is some evidence also that oral sepsis, especially, may be a contributing factor in producing arteriosclerosis and arterial hypertension. It is possible, too, but not proved, that the same factor may play an etiologic rôle in gastric ulcer, cholecystitis and appendicitis. Certainly a close relationship sometimes exists between chronic infection of the gallbladder or appendix on the one hand and slight erosions of the stomach and recurring attacks of hematemesis on the other hand. Infection of the tonsils is apparently the most common cause of enlargement of the deep cervical lymph-nodes near the angle of the jaw.

In some cases focal sepsis, instead of producing definite metastatic lesions, seems to result in a general state of chronic invalidism, characterized by general lassitude, mental depression, headache, neuromuscular and articular pains, febrile attacks, malnutrition and anemia. Occasionally the blood deterioration is so extreme that the clinical picture suggests that of pernicious anemia. Again, in pyorrhea alveolaris, even if there is no direct invasion of the tissues by way of the lymph or blood stream, various functional derangements of the stomach, such as hyperchlorhydria, achylia gastrica, pylorospasm, etc., may arise as a result of the constant swallowing of the purulent secretion. Finally, it seems to have been proved that certain forms of asthma are due, at least in part, to the anaphylactic activity of proteins set free by the autolysis of bacteria lurking in some focus of infection situated in the nose, nasal accessory sinuses, tonsils or elsewhere.

The arthritis arising from focal sepsis may be acute or chronic, and confined to a single joint or more or less general. Occasionally it is suppurative. Endocarditis may be benign or malignant, acute or chronic. Hematogenous infection of the kidneys may result in glomerulonephritis of an acute, subacute or chronic type, and of any degree of severity. Doubtless

many obscure cases of chronic nephritis with an insidious onset are the result of periodic hematogenous infection by bacteria of low virulence. Riesman[1] has cited a number of instances in which a mild but persistent albuminuria was cured by the removal of foci of infection in the tonsils or elsewhere.

The task of locating a focus of infection that is causing systemic disease is often exceedingly difficult and one that may require the combined efforts of an experienced dentist, rhinologist, genitourinary surgeon, gynecologist and bacteriologist.

In cases of suspected oral sepsis, roentgen-ray films should be made and interpreted only by an expert. The removal of teeth or tonsils merely because they are suspected of being septic is never justifiable. While appropriate treatment often gives brilliant results, the prognosis must necessarily be guarded, even when the primary focus can be definitely identified, because the metastases may have already done irreparable damage or may have already become additional sources of systemic infection.

In **treatment** the chief indications are to remove the source of infection and to strengthen the natural defences of the tissues. The latter may be of no little importance, as lowered vitality is frequently a cause as well as a result of systemic infection. Rest, wholesome, easily digestible food, and the use of iron and other tonics are often essential. Vaccines, especially those prepared from the areas of infection (autogenous vaccines), may be of considerable value in conjunction with local treatment.

## PERIDENTAL SEPTIC INFECTION

In recent years much attention has been paid by clinicians to suppurative lesions about the teeth as a source of systemic infection. The two important conditions are *pyorrhea alveolaris* and *chronic alveolar abscess;* both are exceedingly prevalent, especially in adult life. Pyorrhea alveolaris or chronic pericementitis (Riggs' disease) is a suppurative inflammation of the gingival margins involving the peridental membrane and ultimately the osseous structure around the roots of the teeth. The gums are congested, tender to touch, and bleed easily. The breath is offensive. Gradually the gums recede and pockets of pus are formed between them and the teeth. Actual ulceration of the gums frequently occurs, and unless the process is arrested the teeth invariably become loose. Chronic alveolar abscess usually occurs about the root of the tooth, the infection being transmitted from the dental pulp. It may communicate with the mouth by a sinus or it may be enclosed in a capsule, thus constituting the so-called dental granuloma or blind abscess.

Oral sepsis may be due solely to unhygienic conditions of the mouth, but a lowered resistance the result of gastrointestinal disturbances, diabetes, gout, scurvy, etc., strongly favors its occurrence. In many cases faulty dentistry, especially ill-fitting crowns and poor bridge-work, is an important factor. Accumulations of tartar on the surface of the teeth also invite infection by constantly irritating the gums and forming recesses in which particles of food may collect. Various micro-organisms may be found in pyorrhea pockets and dental abscesses, but as a rule streptococci, hemolytic or non-hemolytic predominate. The entameba buccalis described by Barrett, Smith, Bass and others is also frequently present, but there is no definite evidence of its pathogenicity. The non-hemolytic streptococcus (S. viridans) is especially common in the blind alveolar abscess.

Septic processes in the mouth may remain dormant indefinitely; never-

[1] Jour. Amer. Med. Assoc., Dec. 15, 1917.

theless they are always potential sources of mischief. (See Focal Infection, p. 144.) That they are responsible for many cases of rheumatism, arthritis deformans, endocarditis, myocarditis, and even nephritis has been amply demonstrated. It is conceded also that the toxemia from oral sepsis may produce a severe hemolytic anemia, but Hunter's contention that pernicious anemia of the Addison-Biermer type is of this origin has not been generally accepted. Infection of the nose and especially of the maxillary sinuses, hyperplasia of the submaxillary and anterior cervical lymph-nodes, and inflammatory affections of the eye (iritis, keratitis, retrobulbar neuritis) may be secondary to septic foci primary in the tissues of the mouth. Finally, the constant ingestion of pus produced in peridental infections may be the cause of various disorders of digestion.

The diagnosis of pyorrhea alveolaris is, as a rule, easy, but that of aveolar abscess is frequently difficult and requires the services of a specially trained dentist. Roentgenograms are an invaluable aid, but should be made and interpreted only by an expert.

Before concluding that oral sepsis is the sole cause of a given systemic infection other foci of suppuration must be excluded, consequently there are many cases in which the services of specialists other than the dentist may be necessary.

The local treatment of peridental infection falls strictly within the province of the dentist, but the general measures indicated by the various constitutional conditions which may be in part responsible for the lesions in the mouth must be directed by the internist. Only by the cordial co-operation of dentist and internist can the best results be secured. The extraction of teeth is often necessary, but it should be undertaken only when the teeth are so seriously affected as to be useless or when the lesions are clearly the source of systemic disturbances and cannot be otherwise removed. Vaccines of the dominant bacteria may be tried as an adjuvant to other measures although, as a rule, they are not of much service.

## GONOCOCCUS INFECTION

While the lesions of gonorrhea are in many cases confined to the genito-urinary tract, it is now well recognized that the disease is an important cause of many systemic conditions, the latter being produced by the gonococcus alone or by secondary invaders. In chronic cases with lingering infection in the posterior urethra, seminal vesicles or prostate gland it is, as a rule, the secondary invaders (streptococci, staphylococci, etc.), rather than the gonococci, which produces the various metastatic lesions referred to under Focal Infection (see p. 144). Even in acute gonorrhea with systemic infection the ordinary pyogenic organisms may be the chief offenders, although pure cultures of gonococci have been obtained from the blood during life in a considerable number of cases. The blood stream may be invaded by way of the lymphatics or the local bloodvessels (gonorrheal thrombosis). Of the metastatic processes, the most frequent are arthritis and endocarditis, but other conditions such as pericarditis, pleurisy, peritonitis, myositis, phlebitis, certain inflammatory diseases of the eye, and various cutaneous lesions are occasionally observed. In rare instances there is a general gonococcemia without metastases, the condition being characterized by irregular fever, sweats, and chills or, as in cases reported by Thayer and by Dieulafoy, mimicing accurately typhoid fever even to the rash.

*Gonococcal arthritis* occurs in at least 5 per cent. of all cases of gonorrhea. It may develop at any period of the urethritis, although it is comparatively

rare during the first week. In some cases it occurs long after the urethral process has become latent. It is much more common in men than in women. Previous attacks of ordinary rheumatism predispose to it, as do also trauma, excesses of all kinds, exposure to cold and wet, and pregnancy.

The intensity of the joint affection varies considerably in different cases. In the mildest form pain, tenderness and swelling are slight, the last being sometimes scarcely noticeable. In other cases the disease at first closely resembles acute articular rheumatism, but as it proceeds the pyrexia falls within two or three degrees of normal, the migratory tendency disappears and the process becomes fixed in one or two joints, where it runs a tedious and protracted course. In some cases the arthritis is characterized by a persistent brawny swelling, with much infiltration of the surrounding tissues and severe pain, so that the joint is held firmly fixed. Not rarely a chronic hydrops ensues. Occasionally suppuration occurs and results in extensive destruction of the articular surfaces. In chronic cases with foci of mixed or of non-specific infection the changes in the joints may conform to those of atrophic or hypertrophic arthritis deformans. In the more severe forms of gonorrheal arthritis gonococci can often be cultivated from the inflamed joints.

Although the inflammation is monarticular in many cases, polyarthritis is far more common than is generally supposed. The joints affected with greatest frequency are the knee, ankle, wrist, elbow, shoulder and hip. Except in the acute suppurative form the constitutional disturbance is usually mild as contrasted with the local symptoms. The disease often persists for weeks or months, although very mild attacks may subside in a week or ten days. Permanent limitation of movement varying from slight stiffness to complete ankylosis occurs in many cases.

A form of "painful heel" sometimes follows an attack of gonorrhea, usually, but not invariably, after the occurrence of arthritis. The pain appears in the region of the heel on walking and gives rise to a peculiar "tiptoeing gait." Radiographic examination generally reveals an exostosis of the os calcis.

In the **treatment** of gonococcal arthritis measures directed to the original focus of infection in the genitourinary tract are of prime importance. Drugs, as a rule, have little influence on the course of the disease, although salicylates may relieve the pain to some extent. In many cases, however, tonics are called for. Polyvalent vaccines are often of value. In acute cases 10,000,000 cocci may be given every 3 to 4 days and in chronic cases, 50,000,000 to 150,000,000, every 5 to 7 days. The local treatment in the acute stage is that of ordinary rheumatism. Fixation of the joints, preferably by splinting in the most comfortable position, is essential. With the subsidence of the acute stage counterirritation by means of the Paquelin cautery or blisters, stasis hyperemia by the Bier method, "baking" and passive motion are generally the most useful measures. If the joint is greatly distended or if the effusion persists aspiration should be practiced. Recurring accumulations of fluid call for arthrotomy and thorough irrigation of the joint with a solution of mercuric chlorid (1:10,000) or of phenol (1:500). In suppurative arthritis free incision and drainage are indicated. Painful heel is usually relieved by excision of the exostosis.

*Endocarditis* is not a common complication of gonorrhea, although the aggregate number of cases on record is somewhat large. As a rule it occurs in association with arthritis. It may be due to the gonococcus itself, as shown by bacteriologic examinations of the blood during life or of the vegetations after death, or it may be due to the ordinary pyogenic organisms, which have entered the blood from the primary lesion. True gonococcal endo-

carditis is usually malignant, but probably not always so, for cases with recovery have been reported even after the repeated demonstration of gonococci in the blood. The aortic and mitral valves are most often affected, although right-sided involvement seems to be more common than in simple endocarditis. The vegetations as seen after death are in most cases extremely luxuriant and friable. Myocarditis and pericarditis frequently accompany the endocarditis. *Pericarditis* alone has been reported in a few instances.

*Pleurisy* of gonococcal origin is rare, as is also *phlebitis*. A considerable number of cases of diffuse gonococcal *peritonitis* are on record. The disease occurs chiefly in young girls or in women and is usually the result of a direct extension of the infection through the uterus and Fallopian tubes. In rare instances, however, it may be of metastatic origin. Apart from the myositis that frequently occurs in proximity to inflamed joints, *circumscribed suppurative myositis* as an independent lesion has been observed in a few cases. The *kidneys* may be involved by direct extension or more rarely by metastasis. *Metastatic iritis* occurs in from 2 to 5 per cent. of the cases in which there is well-marked arthritis. Metastatic conjunctivitis is occasionally observed. It is usually milder than the form resulting from direct inoculation of the conjunctiva and is bilateral. *Neuritis* is not infrequently associated with arthritis, but it may occur independently. In prostatitis and seminal vesiculitis of gonorrheal origin, various *psychic disturbances*, varying in degree from a slight mental depression to a definite melancholia, are by no means uncommon.

Certain *lesions of the skin*, including different forms of erythema, urticaria, hemorrhagic and bullous exanthema and hyperkeratosis (non-inflammatory horny papules or crust-like lesions) are occasionally observed in gonorrhea, but the nature of the association is not clear.

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## ERYSIPELAS

**Definition.**—Erysipelas is an acute, infectious, communicable disease, due to the hemolytic streptococcus, and characterized by a rapidly spreading inflammation of the skin, or, more rarely, of a mucous membrane, and toxemia with pronounced pyrexia.

**Etiology.**—The disease is excited by a streptococcus, isolated by Fehleisen[1] in 1883, and now known to be a strain of Streptococcus hæmolyticus, which has attained only a moderate degree of virulence and has acquired a special pathogenicity for the subcutaneous tissues. The organism is found chiefly in the lymph-spaces and lymphatics of the affected tissues and most abundantly at the spreading edge of the inflamed area.

There is no essential difference between so-called surgical erysipelas, which results from the infection of an obvious wound, and so-called idiopathic erysipelas, which attacks principally the face and appears to develop spontaneously, since in the latter there is always some inconspicuous breach of surface, such as a fissure at the angle of the nose or at the corner of the mouth, which serves as the infection atrium. As Holmes[2] has pointed out many cases of facial erysipelas can be traced to antecedent infection of the nose or accessory nasal sinuses. The disease is undoubtedly communicable, but the degree of its contagiousness is limited and its transmission from one individual to another in a medical ward of a hospital is rarely observed.

[1] Aetiologie des Erysipels, Berlin, 1883.
[2] Annals of Otol., Rhin. and Laryngol., 1907, xvi, 457.

Wounded persons and puerperal women, however, are very susceptible to infection, and before the general adoption of asepticism outbreaks of erysipelas frequently occurred in the surgical and lying-in wards of hospitals.

Erysipelas may occur at any age, but the ordinary facial variety is most common between the twentieth and fiftieth years. It affects males somewhat more frequently than females. Certain individuals and certain families seem to show a special disposition to the disease. Season is not without influence, the maximum number of cases and the highest mortality occurring in the colder months of the year. Lowered vitality, whether from unfavorable surroundings and unwholesome food, alcoholism, or chronic disease, such as nephritis, cirrhosis of the liver, etc., is an important predisposing factor. An attack of erysipelas confers no immunity.

**Morbid Anatomy.**—Much of the redness and swelling observed during life disappears after death. Microscopic examination of the affected part reveals edematous infiltration of the tissues, an abundance of streptococci in the lymph-spaces and lymphatics, great numbers of small mononuclear wandering cells, and colliquative degeneration of the rete-cells and connective tissue. The extension of the process is by way of the lymphatics. In severe cases the inflamed tissues may undergo necrosis with the formation of abscesses or even of gangrenous sloughs. The changes in the internal organs are such as result from other severe infections.

**Symptoms.**—The *incubation period* is, as a rule, from 3 to 7 days. The constitutional disturbance and the local lesion usually appear simultaneously, although sometimes the one precedes the other by a few hours. In typical cases the onset is sudden and marked by a chill, a rapid rise of temperature to 104° or 105° F. headache, pain in the limbs, and sometimes vomiting. The temperature often reaches its maximum on the second or third day, and then continues with pronounced oscillations, or sometimes with only slight morning remissions, until the sixth or seventh day when it falls by a rapid lysis or even an actual crisis. It may, however, persist for a much longer period and in this event defervescence is usually gradual. While the pyrexia lasts the pulse is frequent; the tongue is heavily coated; the appetite is lost; the bowels are sluggish; and the urine is scanty and often albuminous. Moderate leucocytosis is the rule. In severe cases the patient may pass into a typhoid condition, with muttering delirium, a feeble dicrotic pulse, a dry brown tongue, diarrhea, and extreme muscular weakness, ending, perhaps, in coma and death.

*Local Symptoms.*—In ordinary facial erysipelas the inflammation usually begins in the neighborhood of the nose, whence it spreads centrifugally in uneven lines over a greater or less surface, not ceasing in many instances until it has involved the greater part of the face and scalp. A peculiarity of the process is its tendency to end at some natural boundary, such as the margin of the hairy scalp or the nape of the neck. The affected area is red, swollen, tense and hot, and where advancing presents an irregular elevated border, which sharply divides the unhealthy from the healthy skin. The color varies from a bright crimson to a dusky red. The surface of the inflamed patch is at first smooth and shining, but it often becomes vesicular or bullous within twenty-four hours. In severe attacks the face may be so much swollen that the features cannot be recognized. Pain is rarely acute, but there is always a sense of smarting and of tension in the affected part. The inflammatory process rarely lasts in one spot more than three or four days, although it is usually spreading to another part while it is fading in the one first attacked. When extension ceases the symptoms, both local and general, rapidly subside, so that in favorable cases the whole duration of the

disease is scarcely more than a week. During convalescence the redness is gradually replaced by a yellowish discoloration and the cuticle ultimately desquamates. When the scalp has been involved the hair often falls, but there is no danger of permanent baldness.

**Variations.**—Sometimes the inflammation is very severe and ends in suppuration or even gangrene of the cellular tissue. Occasionally the disease extends from the face to the trunk and continues to spread until it has invaded in succession nearly every part of the skin (*migratory erysipelas*). In such cases the duration of the attack may be prolonged to three or four weeks. Erysipelas may spread by continuity to the mucous membrane of the nose, mouth or throat, or may attack one of these parts primarily. This type of the disease differs from an ordinary catarrhal inflammation in being intensely painful and accompanied by marked swelling of the mucous membrane, high fever, and tumefaction of the regional lymph-nodes. Suffocation may occur from a sudden involvement of the larynx. The so-called angina of Ludwig is probably an example of erysipelatous pharyngitis. In the new-born erysipelas may begin at the navel and then spread over the abdomen to the genitals or thighs.

**Complications and Sequelæ.**—*Superficial abscesses* are common. Occasionally *gangrene* of the *eyelids* or an *orbital cellulitis* supervenes. The latter causes exophthalmos, compression of the central vessels of the retina, and inflammation of the optic nerve, and may result in blindness, or, through an extension of the inflammation to the meninges or the occurrence of sinus thrombosis, in death. *Pneumonia* is somewhat frequent, especially in debilitated subjects. Albuminuria is the rule and *acute nephritis* sometimes occurs. *Malignant endocarditis, pericarditis, pleurisy, meningitis* and *otitis media* may occur, but are comparatively rare. *Pyemia* with metastatic abscesses may ensue. *Arthritis* was observed in 20 of 1,674 cases analyzed by Anders. *Edema of the larynx* occasionally occurs. In drunkards *delirium tremens* may develop. *Relapses* and *recurrences* are very common.

Occasionally, an attack of erysipelas results in the cure of chronic eczema, lupus, or even a malignant tumor, especially sarcoma (*érysipèle salutaire*).

**Diagnosis.**—The diagnosis is usually easy. From *acute eczema* the disease may be distinguished by the sharply defined brawny margin, often with tongue-like extensions, the marked swelling, the fever, and the absence of pronounced itching. *Anthrax* may simulate erysipelas, but the former usually results in the formation of a central black eschar, surrounded by a ring of vesicles which is distinctive. In doubtful cases recourse should be had to a bacteriologic examination.

**Prognosis.**—In robust adults erysipelas usually ends in complete and rapid recovery. In the aged, in newborn infants, in alcoholic subjects, and in persons suffering from chronic nephritis or any wasting disease the prognosis is grave. In 1,084 cases analyzed by Pontano[1] the mortality was 8 per cent. and in 800 cases analyzed by Erdman[2] it was 11.6 per cent. The mortality is higher in erysipelas of the body than in that of the face.

**Treatment.** *Prophylaxis.*—Isolation of the patient and the incineration of all dressings are important prophylactic measures. Extra precaution against infection must be taken in the case of surgical or parturient patients, owing to their great susceptibility to the disease.

*Internal Treatment.*—A supporting liquid or semi-liquid diet is required. High fever is best controlled by cold sponging or the cold pack. Restlessness, delirium and insomnia call for the application of an ice-bag to the head

[1] Policlinico, 1912, xix, No. 1.
[2] Jour. Amer. Med. Assoc., Dec. 6, 1913.

and the administration of bromids or chloral. Digitalis, caffein and strychnin are the most reliable remedies in combating circulatory weakness. Of the special remedies that have been recommended from time to time, ferric chlorid, first suggested by Bell in 1851, has remained the longest in favor. From 10 to 20 minims (0.6–1.2 mils) may be given every three hours. While it is apparently of some service, the drug is by no means a specific and should be withdrawn if it disturbs digestion.

*Local Treatment.*—The most useful local applications are lotions of ice-cold lead-water and laudanum, of a saturated solution of magnesium sulphate, and of a saturated solution of boric acid; and ointments of ichthyol (30 to 40 per cent.) and of colloidal silver (unguentum credé—15 per cent.). The application of lunar caustic in a ring or of iodin in a broad band about two inches in advance of the inflamed area sometimes arrests the spread of the disease in migratory erysipelas, but more frequently it is unsuccessful.

Local abscesses should be treated surgically. Should the larynx become involved the constant sucking of ice may control the swelling, but if this measure fails and dyspnea becomes pronounced recourse should be had to scarification of the edematous tissue, tracheotomy or intubation.

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## TETANUS

(Lock-jaw)

**Definition.**—Tetanus is a grave infectious disease characterized by painful spasms of the muscles and caused by a toxin elaborated by Bacillus tetani at the site of inoculation, which is always a wound or some other break of the surface.

**Etiology.**—The bacillus of tetanus was discovered by Nicolaier in 1885 and isolated in pure culture by Kitasato in 1889. It is found in the superficial layers of the soil, especially in garden earth, in manure, in street dirt, on fruits and vegetables exposed to dust, in the feces of horses and other herbivorous animals, and not infrequently in the feces of man. Although it is widely distributed it seems to be much more prevalent in some localities than in others. Northern New York, Long Island, Virginia, Georgia, Louisiana, and southern California in the United States and northern France and Belgium in Europe are important tetaniferous regions.

The organism is a slightly motile, spore-forming, anaërobic bacillus, frequently swollen at one end, like a drum stick, owing to the presence of a rounded spore. It stains with ordinary anilin dyes, is Gram-positive, and develops rapidly in gelatin and bouillon, if excluded from oxygen. It is readily destroyed by water at 65° C., but its spores are extremely resistant to heat, drying and the various chemical disinfectants.

Access of the bacillus to the human body is gained almost exclusively through external wounds or abrasions. Tetanic infection, however, does not always follow inoculation, probably because all wounds do not provide the requisite anaërobic condition. The association of certain other bacteria, such as the pus cocci, greatly favors the occurrence of infection by consuming oxygen and thus permitting the tetanus bacilli to develop. Tetanus occurs most frequently after punctured or contused wounds with penetration of foreign matter, especially garden earth, street dirt or stable refuse. Lacerations caused by blank cartridges, fire-crackers, toy-pistols, etc., are particularly dangerous. In the period between 1903 and 1905 Fourth of July celebrations resulted in no less than 1119 cases of tetanus, of which 991 were

fatal. Wounds of the lower limbs are the most liable and those of the chest and abdomen the least liable to infection. The disease is a rare complication of vaccination, being usually due to secondary infection of the wound, and seldom, to contamination of the vaccine virus. It has occasionally followed the use of the hypodermic needle. A number of hospital outbreaks have been traceable to the use of infected catgut sutures. At least 30 cases of tetanus from the subcutaneous injection of unsterilized gelatin solutions have been recorded. The disease has resulted from the injection of antidiphtheria serum drawn from horses in the period of incubation preceding the active symptoms of tetanus caused by natural infection (Hektoen). It sometimes occurs in women soon after childbirth from infection of the uterus (*puerperal tetanus*) and in the newborn from infection of the umbilical ulcer (*tetanus neonatorum*). Occasionally no breach of the surface can be discovered (*cryptogenic* or *idiopathic tetanus*). In such cases it is probable that infection has occurred through an inconspicuous wound, perhaps one already healed, or through an abrasion of a mucous membrane. Possibly, as Semple[1] maintains, spores may enter into insignificant excoriations, remain in the healed area for months, and then become active as a result of exposure to cold, fatigue or bruising of the part. In rare instances the infection-atrium may be in the middle ear, urethra, rectum or an infected tooth. It is very unlikely that the disease ever arises spontaneously without some breach of the surface. The tetanus patient himself is a negligible factor in the spread of the disease, although wound to wound infection is not unknown.

Tetanus is much more common in hot than in cold climates. Negroes are particularly susceptible. Males, owing to their greater liability to wounds, are more often affected than females. Many observers believe that sudden changes of temperature favor the development of the disease in wounded persons. The average incidence of tetanus to the total number of wounded in modern warfare is from 1.5 to 2 per cent., but at one period of the recent European war (October, 1914) the incidence in the British forces was no less than 32 per 1000.

**Pathogenesis and Morbid Anatomy.**—The bacillus of tetanus, like that of diphtheria, remains localized at or near the point of inoculation. It does not enter the blood or internal organs, although, according to Porter and Richardson,[2] it may be found in the lymph-nodes adjacent to the infected wound. The chief manifestations of the disease are due to an intensely virulent and rapidly diffusible toxin (tetanospasmin), which has a strong affinity for nerve tissues. The researches of Meyer and Ransom[3] and others have shown that this poison travels from the periphery, by way of the axis cylinders of the nerves or the perineural lymphatics, to the spinal cord and medulla, where it produces such extreme hyperexcitability of the ganglion cells that tonic convulsions ensue. The fact that the nerves rather than the blood stream convey the toxin to the central nervous system offers an explanation of the occurrence, in certain cases, of the first tetanic symptoms in the muscles adjacent to the wound and also of the long incubation period frequently observed in tetanus. A certain amount of the toxin, however, enters the blood and eventually reaches the spinal cord through other nerve-fibers. Apparently no toxin ever reaches the central nervous system directly from the blood. The toxin itself, free of bacteria, when introduced into the body through a wound, is capable of producing all the phenomena of the disease.

[1] Lancet, May 20, 1911.
[2] Boston Med. and Surg. Jour., Dec. 23, 1909.
[3] Arch. f. exper. Path. u. Pharm., 1903, xlix, 369.

In addition to tetanospasmin, the bacillus of tetanus yields a hemolytic toxin (tetanolysin), which is probably of minor importance.

Tetanus produces no conspicuous anatomical lesions. Areas of hyperemia may be found in the spinal cord and the microscope usually shows retrograde changes in the ganglion-cells similar to those occurring in other intoxications. Occasionally in protracted cases peripheral neuritis supervenes (Hnatek[1]).

**Period of Incubation.**—The period elapsing between the reception of the wound and the occurrence of symptoms is usually from 5 to 15 days. Not rarely, however, it is much longer, and sometimes two, three or even four months pass before the disease develops. This *delayed* or *tardy tetanus*, as it is termed, has been fairly common since antitoxic serum has come into general use as a prophylactic remedy. It may occur after complete healing of the wound, but usually it develops in connection with some secondary operation in the region of the initial injury, persistent suppuration or the mobilization or discharge of a foreign body or sequestrum.

**Symptoms.**—As a rule, the earliest symptoms are a feeling of soreness and stiffness in the back of the neck and about the jaws. These sensations are soon followed by tonic spasm of the muscles of mastication, resulting in an inability to open the mouth (*lock-jaw* or *trismus*). By degrees the spasmodic contraction extends to other muscles, especially those of the back, face, and abdomen, and ultimately nearly every voluntary muscle of the body may be more or less affected, although those of the forearm and hand usually escape. In exceptional cases contractions begin in the muscles of the wounded part, and then extending upward become general (*tetanus ascendens*).

When the disease is fully developed, the brows are contracted as in the expression of distress, while the angles of the mouth are drawn up as in laughing (*risus sardonicus*); the teeth are clenched, the abdominal muscles are tense, and the whole body is rigidly straight (*orthotonos*), or more frequently, is arched backwards so that only the occiput and the heels touch the bed (*opisthotonos*). Very rarely the body is curved forward (emprosthotonos) or to one side (pleurosthotonos) instead of backward. Dragging pain at the base of the chest and more or less dyspnea are often experienced. Attempts at swallowing sometimes excite spasmodic contractions of the muscles of deglutition. At longer or shorter intervals the persistent muscular rigidity is temporarily intensified by cramp-like paroxysms attended by severe pain and, perhaps, profuse perspiration. These clonic seizures are excited by slight peripheral irritation arising from without or from within the body. Occasionally they are so violent as almost to hurl the patient from his bed. In a few instances individual muscles, such as the rectus abdominis, have been torn by the force of the contractions. Exhaustion and emaciation are frequently pronounced, and may continue even after the spasms have been controlled. The temperature is variable. Sometimes it is fairly high (103°–104° F.), especially during the paroxysms, and just before death it may rise to 108° F. or even higher. Mild attacks are not rarely afebrile. The tongue is coated, the bowels are inactive, and the pulse is somewhat accelerated. The mind remains clear to the end. The disease may terminate fatally in less than twenty-four hours, or it may continue for a week or longer. After the lapse of a week, however, each additional day should increase the hope of recovery. Death may be due to exhaustion, to heart-failure or to asphyxia consequent on spasm of the respiratory or laryngeal muscles.

*Chronic Tetanus.*—In this form of the disease, which is not uncommon,

[1] Wien. med. Woch., 1905, 55, 997.

the symptoms appear, as a rule, late after injury, develop gradually, and are less severe than those of acute tetanus. The course of the disease is usually long, sometimes extending over several weeks.

*Localized Tetanus.*—In some cases the spasms begin in the muscles of the injured part and remain localized. Pain, often referred to as "rheumatic," usually precedes the contractions. A single group of muscles, one limb, or two corresponding limbs may be affected. Occasionally in wounds of the trunk the rigidity is confined to the muscles of the abdominal wall or back or to those of respiration or deglutition.

*Cephalic tetanus* (Head-tetanus of Rose) is a comparatively rare form of localized tetanus. It results from injuries of the head or face and is characterized by trismus, dysphagia, dyspnea, and, not rarely, by paralysis of the facial, oculomotor, abducens, hypoglossal or trochlear nerve. Spasm of the larynx is sometimes an urgent symptom. Localized tetanus is usually, but not invariably, tardy in developing and more or less chronic.

*Tetanus neonatorum* is caused by infection of the umbilical wound. It was formerly very common in certain regions, especially in the southern United States, and in the West Indies, where in some islands one-half of the negro infants died of the disease. It still prevails in warm countries among the poor and illiterate, but its ravages have been greatly diminished by the instruction of midwives in the hygienic care of the umbilical wound.

**Diagnosis.**—The spasms of *strychnin poisoning* resemble those of tetanus but they come on more suddenly, attack by preference the muscles of the extremities, affect the jaw muscles very late, if at all, are separated by intervals of complete relaxation, and are quickly followed by death or recovery. *Tetany* is distinguished by the difference in its etiologic factors, the commencement of the spasms in the extremities, the absence of trismus, and the peculiar attitude of the hands, the thumbs and fingers usually being adducted, the proximal phalanges flexed, and the distal phalanges extended ("accoucher's hand"). In *hydrophobia* there is a history of the bite of a supposedly rabid animal, the spasms affect chiefly the muscles of deglutition and respiration, there are marked psychic symptoms and trismus, persistent rigidity, and opisthotonos are absent. *Hysterical convulsions* occur especially in neurotic women, there is no history of a primary wound, consciousness is usually affected, emotional disturbances are common, the spasms often begin suddenly, and other stigmata of hysteria may, as a rule, be elicited.

**Prognosis.**—Tetanus is a grave disease. The outlook is particularly gloomy when the symptoms develop rapidly, the muscular rigidity is widespread and the clonic spasms follow one another in rapid succession. On the other hand, there is more hope of a successful issue when the rigidity develops slowly and shows little tendency to spread beyond the muscles of the neck and jaw. Generally, the longer the period of incubation the greater the likelihood of recovery. Of 858 cases analyzed by Anders and Morgan,[1] the mortality was 66.4 per cent. in 384 with an incubation of a week or less; 48.9 per cent. in 333 with an incubation of 2 weeks; and 40.4 per cent. in 141 with an incubation of three weeks or more. The mortality in 568 acute cases (those lasting 10 days or less) was 74 per cent., while the mortality in 211 more chronic cases (those lasting over 15 days) was only 8.5 per cent. The analyses made by Sir David Bruce[2] of the cases of tetanus occurring in the British armies and treated in the home military hospitals are of interest. The first series of 231 cases with an average incubation period of 13.4 gives a mortality 57.7 per cent.; the third series of 200 cases with an average incu-

[1] Jour. Amer. Med. Assoc., July 29, 1905.
[2] Lancet, 1915, 1916, 1917, 1918, 1919.

bation period of 30.6 days gives a mortality of 36.5 per cent.; the fifth series of 100 cases with an average incubation period of 67 days gives a mortality of only 19 per cent. and the eleventh series of 100 cases with an average incubation period of 54.8 days gives a mortality of 26.0 per cent.

At the present time localized tetanus usually ends in recovery. In three series of cases, one of 29, another of 13 and a third of 14 cases, analyzed by Bruce there were no deaths. The mortality of tetanus neonatorum and of puerperal tetanus is over 90 per cent. When recovery occurs in tetanus, it is usually complete. Stiffness of the muscles, however, may persist for weeks or months. Peripheral neuritis is an occasional sequel. Parotid abscess has also been observed. Relapses are not uncommon, and may occur after an interval of several weeks and then prove fatal.

**Treatment.**—Prophylactic treatment is of supreme importance. Suspicious wounds should be widely opened, freed of foreign bodies and all sloughing tissue, irrigated with a solution of hydrogen dioxid and then swabbed out with tincture of iodin (3 per cent.). They should never be cauterized, as eschars favor the growth of anaërobic bacteria. The value of tetanus antitoxin in neutralizing the tetanus toxin before it has become fixed to the cells of the spinal cord has been amply demonstrated, and therefore this remedy should be used in all cases. Although it is not always successful in preventing the disease, when used early and in sufficient quantity it decidedly lessens the likelihood of infection and, if the latter does occur, tends to mitigate the violence of the attack. In the British army the incidence of tetanus was apparently reduced by universal immunization from 32 per thousand to 2 per thousand. As a prophylactic measure from 500 to 1000 U. S. A. units should be injected subcutaneously as soon as possible and then at weekly intervals until the wound heals. Multiple injections are often required because the protective power of the serum does not usually extend beyond a week or ten days and the incubation period of tetanus is not uncommonly several weeks.

With the appearance of the first signs of the disease the patient should be placed in a darkened, well-ventilated and quiet room, and protected, as far as possible, from all external irritations. The bowels should be moved by salines or castor oil or by enemata. Retention of urine not rarely occurs and requires the use of the catheter. The food should be nutritious, but readily digestible. If swallowing is not possible, food must be introduced into the stomach through a nasal tube passed under chloroform anesthesia. Proctoclysis with normal salt solution is thought to be of service.

The curative power of antitetanic serum is much less certain than its usefulness as a means of prophylaxis, nevertheless most observers believe that it is of value when used promptly and in large doses. It is best administered intrathecally and subcutaneously or intramuscularly. Intravenous injection has had its advocates, but it has been largely discarded on account of the risk of anaphylaxis. Intraneural administration is also recommended and is a rational measure, especially when localized rigidity is an early sign. At least 3000 units should be injected intrathecally, after removal of a requisite amount of cerebrospinal fluid, and the treatment should be repeated daily for four or five days. At the same time from 10,000 to 25,000 units should be administered intramuscularly or subcutaneously, and, unless improvement occurs and is sustained, a similar amount should be injected again in from 18 to 24 hours. The drawback to subcutaneous and intramuscular injections is the extreme slowness of absorption. In cases of ascending tetanus from 500 to 1500 units may be injected into the main nerve-trunk.

Baccelli's treatment, which consists in administering intramuscularly 1 mil of a 1 per cent. solution of phenol every few hours, until 40 to 70 mils in all are given daily, has not met with much favor in the United States or in England (see Memorandum on Tetanus issued by the British War Office[1]).

*Symptomatic treatment* is always required to control the spasms and to secure rest and sleep. The best drugs for the purpose are chloral and bromids, the former in doses of 30 to 40 grains (2.0–1.6 gm.) every six hours and the latter in doses of 1 dram (4.0 gm.) every six hours. Chorbutanol (chloretone) and scopolamin (hyoscin) have also been recommended, but they must be used very cautiously. Morphin is of service when there is severe pain and insomnia. It should not be employed, however, to the exclusion of chloral and bromids. The intraspinal injection of a 25 per cent. solution of magnesium sulphate (1 mil for every 20 pounds of body-weight) has been employed to some extent as a means of depressing the spinal cord, but in a number of instances it has caused an alarming depression of respiration. If the paroxysms are so violent that they threaten death by asphyxia or exhaustion chloroform inhalations should be used. Stimulants (digitalis, caffein, camphor) are frequently required to combat exhaustion and circulatory failure.

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## ANTHRAX

(Malignant Pustule; Wool Sorters' Disease; Splenic Fever; Charbon)

**Definition.**—Anthrax is a specific contagious disease of lower animals, especially cattle and sheep, communicable to man, due to Bacillus anthracis, and acquired by direct inoculation through a cutaneous wound or by inhalation or ingestion of the bacillus or its spores.

**Etiology.**—Anthrax is widespread, but is especially prevalent in China, Russia, Turkey, South America and South Africa. In cattle and sheep infection is chiefly by way of the alimentary canal, the animals acquiring the disease, as a rule, by swallowing anthrax spores while grazing in infected pastures. In this country several outbreaks among herds have been traced to the inundation of pasture land by streams which received refuse from tanneries using infected hides. A pasture once infected may remain so for many years. While cattle and sheep are especially susceptible, horses, pigs, goats and even carnivorous animals are sometimes affected. Infection in animals is only rarely acquired by direct inoculation through abrasions of the skin.

In human beings anthrax occurs especially among herdsmen, stablemen, tanners, leather workers, wool sorters, brush makers and butchers, and in this country, at least, the large majority of cases are the result of cutaneous inoculation. In some instances the disease has been traced to the use of shaving brushes made of the bristles of infected animals. Indeed, since 1914 shaving wounds have become one of the commonest sources of infection. Possibly flies or other insects may occasionally be the means of transmitting the disease from animals to man. A few cases of laboratory infection have been recorded. Direct transmission from one human being to another is almost unknown. The form of anthrax known in England as wool sorters' disease is due to the inhalation of spores contained in dust arising from the wool of infected animals. Infection by way of the alimentary canal is rare

[1] Brit. Med. Jour., Nov. 11, 1916.

in man, but it may occur by eating the meat (insufficiently cooked) or drinking the milk of infected animals. One attack of anthrax confers a partial immunity.

Bacillus anthracis is a comparatively large rod-shaped, non-motile organism, staining readily with ordinary anilin dyes, and when grown in artificial culture media, producing remarkably long thread-like projections. Outside of the body in the presence of free oxygen it forms spores, which are among the most resistant of all pathogenic organisms. In infected human beings the bacilli may be found always at or near the primary lesion and often, when the disease is advanced, in the blood, in serous effusions and even in the urine. Susceptible animals may be successfully vaccinated against anthrax by inoculation with attenuated cultures of anthrax bacilli, and the serum of animals thus actively immunized possesses protective and therapeutic properties.

**Pathology.**—Depending on the avenue of infection there are three principal forms of the disease: the cutaneous, the respiratory and the intestinal. The characteristic lesion of the *cutaneous form* is a localized boil or abscess, somewhat resembling an ordinary furuncle or carbuncle. The process often halts at the skin and subcutaneous tissues, and may even subside spontaneously, but sometimes it progresses into a veritable anthrax septicemia. The bacilli at first are apparently confined to the lymph channels, but later in the disease they are found in the blood stream. Occasionally there is no definite pustule at the point of inoculation, the initial lesion being represented by a rapidly spreading inflammatory edema, and in this event there is almost always a fatal systemic infection.

*Pulmonary anthrax* is characterized by a severe bronchitis, lobular or confluent pneumonia, swelling of the bronchial lymph-nodes, sero-fibrinous or hemorrhagic pleurisy, hemorrhagic infiltration of the mediastinal tissues and the usual lesions of a general anthrax infection. In *intestinal anthrax*, the small intestine, especially the jejunum, is the seat of small foci of inflammatory edema and hemorrhage, sometimes progressing to central sloughing and ulceration, the mesenteric lymph-nodes are swollen and hemorrhagic, and evidences of an acute general infection are also present. In fatal general anthrax the viscera are the seat of cloudy swelling; hemorrhages are frequently seen in the mucous and serous membranes, lymph-nodes and various organs, and the spleen is often swollen, soft and dark, its peculiar appearance suggesting the synonym "splenic fever." Hemorrhagic meningitis due to anthrax is not very uncommon and occasionally it occurs without any recognizable external lesion.

**Symptoms.**—In the *cutaneous form* (malignant pustule), after a period of incubation lasting from 1 to 3 days, a small red papule, attended by a slight pricking or burning sensation, develops at the site of inoculation, which is almost always on one of the exposed parts, such as the face, the neck or an arm. The papule rapidly increases in size and soon becomes a flattened vesicle, filled with clear or perhaps sanious fluid and surrounded by a zone of redness, swelling and induration. Within 24 or 36 hours the vesicle ruptures and is replaced by a brownish or blackish depressed eschar, which increases in extent and becomes surrounded by an irregular ring of smaller vesicles. Meanwhile a brawny edema rapidly spreads over the adjacent parts, affecting, perhaps, one side of the face and neck or an entire arm. Swelling of the regional lymph nodes may also occur. Despite the extensive edema there is little or no pain in the affected part. Constitutional disturbance may be inconspicuous, especially if the process remains localized in the skin and subcutaneous tissues, but in many cases after two or three days or possibly a

week, septicemia ensues with chilliness, anorexia, headache, restlessness, increasing weakness and rapidity of the pulse and prostration. Occasionally, meningitis develops and in this event the spinal fluid becomes bloody and rich in anthrax bacilli (Babes, Risel, Czhiarz, Gilmour and Campbell, Roscoe and others). The temperature is variable; it may be high (103°–104° F.), although it is often normal or subnormal throughout. In favorable cases the general symptoms, if present, subside and the eschar is cast off, leaving a suppurating cavity, which eventually heals by cicatrization.

Occasionally, instead of a vesiculopapular lesion, there is an intense rapidly spreading edema with the formation of superficial blebs and perhaps small areas of gangrene (*anthrax edema*). In this form of anthrax fatal systemic infection is the rule.

*Pulmonary anthrax* is characterized by chilliness or, less frequently, a definite chill, a sense of oppression in the chest, difficult breathing, cough with bloody expectoration, prostration and collapse. The temperature is rarely high; vomiting is common and occasionally there is diarrhea; râles are usually audible over the chest, but definite signs of pulmonary consolidation cannot often be elicited. Death occurs in the majority of cases, the duration varying from 24 hours to three or four days.

In *intestinal anthrax* the usual symptoms are chilliness, malaise, slight fever, headache, abdominal pains, tympanites, vomiting and diarrhea, the stools frequently containing blood. Collapse rapidly supervenes and death usually results in from two to five days, the end sometimes being preceded by delirium, convulsions and coma.

**Diagnosis.**—The diagnosis of ordinary cutaneous anthrax is not difficult. It is based in the early stages on the absence of pain and suppuration and later on the central depression and blackish eschar, the circle of vesicles and the wide area of swelling and induration. The patient's occupation may also afford an important clue. In doubtful cases careful search should be made at once for the bacilli. Internal anthrax is likely to pass unrecognized unless the patient is known to have been exposed to the virus of the disease.

**Prognosis.**—The disease is always of serious import, although with prompt treatment many patients recover. Lesions on the neck or about the eyelids are more dangerous than those affecting the forehead or an upper extremity. The presence of the bacilli in the circulation, as shown by blood cultures, is a grave indication. The prognosis is always hopeful, however, so long as the pulse remains full and only moderately rapid and other signs of general intoxication are wanting. The death-rate in cutaneous anthrax, although formerly estimated at 25 per cent., probably does not exceed 10 per cent. under modern treatment. However, in 33 cases of anthrax from shaving-brush infection the mortality was 64 per cent.[1] The death-rate in internal anthrax is still very high, 80 or 90 per cent.

**Treatment.**—Preventive measures include rigid inspection of live stock and quarantine of infected animals; deep burial under quick lime of all infected carcasses; prophylactic vaccination of animals exposed to infection; disinfection of hides, wool, etc., imported from regions where the disease is prevalent; enforcement of proper sanitary regulations by employers of men who handle dangerous materials; prompt disinfection of all wounds in persons who are exposed to infection; and incineration or thorough disinfection of the excretions and discharges of anthrax patients and of all articles soiled therewith.

Shaving brushes may be rendered safe by boiling or by soaking for four hours in a 10 per cent. dilution of liquor formaldehydi at 110° F.

[1] U. S. Pub. Health Rep., July 12, 1918.

Opinions differ as to the advisability of radical local treatment in cutaneous anthrax. Some surgeons advise against excision of the specific lesions contending that it favors rather than hinders the spread of the disease. On the other hand many surgeons, probably the majority, believe that better results are secured by immediately excising the local focus of infection, swabbing the wound with pure phenol and then dressing it with hot antiseptic fomentations, or, if ablation is not feasible, by making crucial incisions into the infected area, treating the wound with phenol, chlorin solution or tincture of iodin, and then dressing the part with hot antiseptic fomentations. Injections of diluted phenol (5 per cent.) at many points around the focus of infection are also recommended.

Whatever local treament is employed, Sclavo's antianthrax serum should be given intramuscularly or intravenously, in doses of 50 to 150 mils, and repeated in 24 hours, if there is no improvement. In 164 cases in Italians treated by Sclavo with serum the mortality was only 6 per cent., in contrast to 24 per cent., the rate of all cases treated in Italy over a period of 15 years (Legge[1]). Graham[2] and Regan[3] report very favorably upon injections of antianthrax serum into the indurated border of the pustule as an adjuvant to the employment of serum intravenously and to the exclusion of excision. A total dose of 10 mils may be injected two or three times in the twenty-four hours, the needle being inserted at two or three points. Kraus,[4] chief bacteriologist of the National Department of Health, Argentina, has reported a mortality of only 5 per cent. in 200 cases treated by intramuscular or intravenous injections of normal beef serum (30 to 50 mils, repeated in 12, 24, or 36 hours, as the case required). The serum is heated twice for half an hour at 56° C. before injection. Kolmer,[5] however, has found beef serum without demonstrable protective or curative value in experimental anthrax infections in mice and rabbits. The general supporting treatment recommended in other grave infections is required in all cases of anthrax.

## GLANDERS

(Farcy; Malleus)

**Definition.**—Glanders is an infectious and highly contagious disease of horses, mules, and other equidæ, communicable to man, caused by Bacillus mallei, and characterized by nodular foci of inflammation and suppuration in the respiratory tract, skin, subcutaneous tissue and muscles, and often by a rapidly fatal general septicemia.

**Etiology.**—Man usually acquires the disease by contact with the nasal discharge or saliva of an infected horse, the bacillus entering the body through an abrasion of the skin or an exposed mucous membrane, such as that of the nose, eye or mouth. The large majority of cases occur in hostlers, veterinarians, farmers, and others whose occupations bring them in intimate contact with horses. A number of instances of laboratory infection with pure cultures of the bacillus have been recorded. Infection by way of the digestive tract is possible, but apparently rare. The period of incubation varies from a few days to several weeks.

[1] Brit. Med. Jour., 1905, i, 589.
[2] New York Med. Jour., Dec. 11, 1920.
[3] Jour. Amer. Med. Assoc., Dec. 17, 1921.
[4] Prensa Medica Argentina, April 10, 1918.
[5] Jour. Infect. Dis., 1920, 26, 148.

The *Bacillus mallei* is a small, non-motile rod about as long as the tubercle bacillus, but somewhat thicker. It stains with ordinary anilin dyes, is readily decolorized by Gram's method, and grows well on all the ordinary culture media.

**Morbid Anatomy.**—Infection is followed by the production of inflammatory nodules, which tend to soften and form ulcers. Macroscopically the glanders nodule resembles somewhat the tubercle, although in man there is little to distinguish it histologically from a simple inflammatory process. Two forms of the disease are recognized, one affecting the respiratory tract, especially the nostrils, and known as *glanders;* the other affecting the subcutaneous tissues, especially the superficial lymph vessels and nodes, and known as *farcy.* The two forms are often associated and after death foci of suppuration and necrosis may be found in almost every portion of the body. In addition to nodules and ulcers in the skin and mucous membrane of the nose, larynx and trachea, and nodules and abscesses in the muscles and internal organs, the findings usually include metastatic lobular pneumonia, sero-sanguinolent effusions into the serous sacs, and the degenerative changes in the viscera common to all septicemic affections.

In the horse the disease is more often chronic than acute and is especially marked, as a rule, in the nostrils and trachea, the chief clinical features being enlargement of the submaxillary lymph-nodes; discharge from the nose and sluggish ulceration of the nasal mucosa; thickening of the superficial lymphatics, with small nodules under the skin, "farcy buds;" and edematous swellings in various parts of the body.

**Symptoms.**—Acute and chronic forms of both glanders and farcy occur in man.

*Acute glanders* begins somewhat abruptly with malaise, chills, severe pains in the muscles and joints, prostration and a moderately high, irregular temperature, the diagnosis at first usually inclining toward septicemia or acute rheumatism. Presently, however, more characteristic symptoms make their appearance, the most important of these being: (1) painful swelling of the nasal mucous membrane, with a purulent blood-streaked discharge from the nose and enlargement and tenderness of the submaxillary and cervical lymph-nodes; (2) diffuse erysipelatoid swellings about the face or, less frequently on the limbs; (3) a more or less generalized eruption of pink papules, which become flat vesicles and then pustules or bullæ, and which, therefore, may be mistaken for smallpox; and (4) the occurrence in the subcutaneous tissue and muscles of hard, painful swellings, which soon break down, producing ulcers with ragged margins and suppurating floors. Gangrenous foci in the skin are also frequently observed. The patient passes into a typhoid condition, pneumonia often supervenes, and the disease ends fatally, usually in from a few days to two weeks.

*Chronic glanders* develops insidiously as a sequel of chronic farcy or as a primary condition. The symptoms resemble those of syphilitic rhinitis. There is more or less pain in and about the nose, with a purulent, often sanious discharge, and ulceration of the nasal mucosa, not rarely proceeding to caries of the bone and even perforation of the septum. Sometimes ulcers appear also in the throat, larynx and trachea, causing dysphagia, hoarseness and cough. The constitutional symptoms are less severe than those of the acute form, although the latter may supervene. The duration varies from a few months to several years.

*Acute farcy* differs from acute glanders principally in the absence of any involvement of the nasal mucous membrane. A phlegmonous inflammation develops at the site of infection and is followed by a deep foul ulcer. The

inflammation extends along the lymphatics, forming subcutaneous nodules known as "farcy buds." Multiple intramuscular abscesses, a diffuse pustular eruption, erysipelatous swellings, and foci of gangrene occur as in acute glanders and the general symptoms are those of profound sepsis. Death occurs in from 3 to 6 weeks.

*Chronic farcy* presents the local lesions of acute farcy, but with much less reaction in the skin and surrounding tissues and less constitutional disturbance. In the course of several weeks, however, multiple abscesses appear in the muscles, pursue a more or less chronic course, and finally break down, leaving fistulæ or indolent ulcers. As a result there is emaciation, with marked debility. The disease may persist for years and finally prove fatal through exhaustion, or, more frequently, through an outburst of acute glanders. In other cases, after several months, recovery may ensue.

**Diagnosis.**—The occupation of the patient is of paramount importance, as in many cases the disease cannot be recognized from the clinical picture alone. Acute forms are most likely to be mistaken for septicopyemia or smallpox, and chronic forms, especially chronic glanders, for syphilis or tuberculosis. In all doubtful cases search should be made for the Bacillus mallei or, much better, some of the suspected discharge or a fragment of diseased tissue should be inoculated intraperitoneally into an adult male guinea-pig (Strauss' test). At the end of the second day, if the case is one of glanders, the animal's testicles become swollen, and in the course of two or three weeks it dies of generalized nodular glanders. The *mallein test*, which is similar to the tuberculin test, may also be employed, especially in chronic cases. The agglutination test of McFadyean has been found specific in horses, but only with high dilutions (1 : 500 to 1 : 1,600).

**Prognosis.**—The disease almost always proves fatal. Chronic forms, however, especially chronic farcy, may terminate in recovery.

**Treatment.**—There is no specific treatment. Mallein appears to be of little or no therapeutic value and as yet no curative serum has been perfected. Nodules and abscesses should be widely opened and disinfected with phenol, tincture of iodin, or chlorin solution. Supporting measures similar to those suggested in pyogenic infections are required in all cases. Discharges from the nose and other suppurating foci must be destroyed and every care must be exercised lest the physician himself and others become infected.

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## MALTA FEVER

**(Mediterranean Fever; Undulant Fever)**

**Definition.**—Malta fever is a subacute or chronic specific infectious disease, caused by *Micrococcus melitensis*, and characterized by repeated attacks of fever alternating with periods of apyrexia and by enlargement of the spleen, neuralgic pains, swelling of various joints, profuse sweating, a specific serum reaction, progressive weakness and anemia.

**Etiology.**—The disease is endemic in Malta and in the Mediterranean basin generally, and cases have been reported in India, South Africa, South America, the West Indies, and the Philippine Islands. It occurs at all periods of life, but persons between the ages of 10 and 40 years are most susceptible. According to Bruce one attack confers immunity.

The causative factor, which was discovered by Bruce in 1886, is *Micrococcus melitensis*, a minute, slightly oval, non-motile organism. It is found

in the blood, spleen, lymph-nodes, kidneys and liver, and leaves the body in the urine, milk and feces. It is very resistant, and will live in dust or water for long periods. The Mediterranean Fever Commission (1904–1907) proved conclusively that Malta Fever is conveyed to man chiefly by milk of infected goats and usually disappears when goat's milk is discarded or is rendered sterile by boiling. Ten per cent. of the goats in Malta were found to be carriers of *M. melitensis*, although the infected animals were, as a rule, apparently healthy. Infection by skin contact or by means of fomites seems never to occur, but the disease may undoubtedly be transmitted by subcutaneous inoculation. A few instances of accidental laboratory infection have been reported. Contaminated food other than goat's milk is probably responsible for a small number of cases. Whether the disease may be spread also by biting insects, by sexual congress (infected urine or vaginal secretions), or by the inhalation of dust that has been contaminated by goat's urine, as has been assumed, has not been definitely determined. Experimentally, the infection may be transmitted to monkeys and domestic animals but only with difficulty to guinea pigs, mice and rabbits.

**Morbid Anatomy.**—The spleen is enlarged, soft and friable, and microscopically presents a great excess of lymphoid tissue. The mesenteric lymph-nodes are also enlarged. The liver, intestines and kidneys are congested. The lungs are congested at the bases and may show areas of bronchopneumonia. *Micrococcus melitensis* is readily isolated from the spleen and usually, but not invariably, from the kidneys, liver, abdominal lymph-nodes and bone-marrow.

**Symptoms.**—After a period of incubation of from 6 to 15 days the disease sets in gradually, as a rule, with headache, pains in the back and limbs, general malaise and fever, which increases each day, with morning remissions, until a maximum temperature of 103° or 104° F. is reached. The remissions of temperature are accompanied by profuse perspiration. The fever lasts from 1 week to 3 or 4 weeks, the temperature gradually falling to normal, where it remains several days, when there is a relapse similar in all respects to the first attack, but often shorter and less severe. This sequence of events is repeated again and again, the duration of the disease varying from 6 or 8 weeks to a year or more. During the pyrexial periods the patient is much depressed and frequently complains of insomnia and of neuralgic pains in various parts of the body, especially in the region of the sciatic nerves. Transient attacks of arthritis, chiefly of the larger joints, are also common. Constipation is the rule, although there is sometimes diarrhea during the first few days of an attack. The spleen is enlarged and tender, the count of white cells in the peripheral blood is normal or slightly reduced, and as a result of the long-continued fever there is usually well-marked secondary anemia, with loss of flesh and strength. Orchitis is a somewhat frequent complication. Cardiac weakness, with palpitation and irregularity of the pulse, may also be observed. Neurasthenia with its varied symptoms is not an uncommon sequel. When improvement occurs the intervals between the fibrile attacks increase until recovery takes place.

Besides the ordinary form of the disease there is rarely a malignant type which is marked by a sudden onset of high temperature and early signs of cardiac failure. Many writers also describe an ambulatory type in which the constitutional symptoms are absent or are very slight and the only evidence of the disease is the presence of agglutinins in the blood and perhaps of the specific organism itself in the blood or urine.

**Diagnosis.**—The recurring waves of pyrexia, profuse sweats, neuralgic pains and joint symptoms are suggestive features, but not sufficient in many

cases to distinguish the disease from typhoid fever, malaria, miliary tuberculosis, septicemia or kala-azar. A positive diagnosis must be based upon the Widal serum reaction with *Micrococcus melitensis*, which may be present as early as the fourth day of the fever, or upon the isolation of the specific cocci from the blood or the urine.

**Prognosis.**—The prognosis is usually good both as regards life and ultimate recovery. The mortality, as a rule, is not more than 2 per cent., although some outbreaks have been reported in which it exceeded 10 per cent.

**Treatment.**—Boiling of goat's milk or abstinence from its use in endemic regions is the most important prophylactic measure, and since its adoption by the military authorities of Malta the disease has virtually disappeared among the troops on the island. Elimination or segregation of infected goats, disinfection of the patient's excreta, especially the urine, and screening the room of the patient against biting insects are also important measures of prevention.

The treatment is symptomatic and as regards general measures much the same as that of typhoid fever. Vaccines and serums have been used, but as yet with little result. Neuralgic pains may be relieved by hot applications and the administration of aspirin or phenacetin, but at times morphin is necessary. The swollen joints should be treated as in rheumatism. During convalescence tonics are indicated.

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## PLAGUE

(Bubonic Plague; Pestis; Black Death)

**Definition.**—Plague is an acute, specific, communicable, disease, caused by *Bacillus pestis* and characterized in its usual form by inflammation of the lymph-nodes (buboes), irregular fever, great prostration, hemorrhagic extravasations in the tissues, and a general bacteremia.

**History.**—Plague is definitely known to have prevailed epidemically since the second century. In the fourteenth century it came into Europe from China under the name of the "black death," and during the succeeding four centuries there were many virulent outbreaks, in some of which from one-fourth to one-half of the population of the country affected succumbed to it. In the Great Plague of London, which occurred in 1665, no less than 70,000 persons are said to have died. From the middle of the nineteenth century the disease remained almost completely in abeyance until 1894 when it broke out in China (Yunnan), and reaching Hong Kong, spread in all directions, gaining a foothold from time to time in nearly every country of the world, including the United States and its dependencies. India has probably been the greatest sufferer, the death-rate in a single decade exceeding 5,000,000. At present the important endemic centers are Thibet, India, Mesopotamia, and central Africa.

Yersin and Kitasato independently discovered the causative organism of plague in 1894, and in 1898. Simonds showed that man acquires the disease chiefly through the bites of fleas which have previously infested diseased rats.

**Etiology.**—The exciting cause of the disease is *Bacillus pestis*, which is found in the lymph, blood, various secretions, and all of the viscera. It is a short, thick, encapsulated, non-motile rod, staining more deeply at the ends than in the center. Although infection can occur through the respiratory

tract (pneumonic type), through the skin by the direct inoculation of an abrasion, and possibly in rare instances through the digestive tract, it almost always occurs through the bite of fleas which have become infected by feeding on plague-stricken rats. When the infected rat dies the fleas find refuge in the hair of other rats or other rodents or attack man. In California the ground-squirrel has been found to be a reservoir for the plague bacillus. Plague epizoötic in rats usually precedes epidemics in human beings by several weeks. The disease is not confined to any special latitude, and insanitary conditions have no relation to its occurrence, except in so far as they favor infection by rats; nor have age, sex or race any etiologic influence. Once plague is firmly established in a community, it usually holds on with great pertinacity, tending to break out again and again.

**Morbid Anatomy.**—The general surface of the body is frequently cyanotic and petechiæ and ecchymoses are commonly observed in the skin, hence the name "black death." The lymph-nodes are swollen, congested, hemorrhagic, and often purulent, these changes being especially pronounced in the nodes tributary to the site of inoculation. The tissues surrounding them are markedly edematous. On opening the body the important findings are multiple hemorrhages, subserous, submucous and interstitial, general congestion of the viscera, enlargement of the spleen, parenchymatous degeneration of the kidneys, liver and heart, and, in many cases, lobular consolidation of the lungs. In one type, primary pneumonic plague, hepatization of the lungs, usually lobular, is the most conspicuous finding. Microscopically, the pulmonary capillaries are greatly distended and the alveoli are filled with desquamated epithelium and a hemorrhagic exudate poor in fibrin. In some cases the patient dies before the occurrence of any exudation and while the lungs are still engorged.

The plague toxin evidently has affinities for many tissues and exerts an intense lytic effect on the endothelium of the capillaries and lymphatics.

**Symptoms.**—The *period* of *incubation* is usually from 3 to 5 days, but it may be as short as 2 days or as long as 14 days. The following varieties of the disease are recognized: (1) Bubonic, (2) pneumonic, (3) septicemic and (4) ambulatory. The large majority of cases belong to the first group.

*Bubonic Plague.*—Prodromal symptoms, such as general malaise, mental depression, muscular pains, etc., are sometimes present, but more frequently the onset is sudden with a rigor, headache, fever and prostration. Vomiting may also occur. The mind is dull, the speech is faltering, the conjunctivæ are injected, the features are drawn, and the expression is either apathetic or anxious. The temperature is, as a rule, high (104°–105° F.), but marked remissions are common. Just before death it may reach 106° or 107° F. The pulse is quickened, often out of proportion to the fever, and while full and tense at first, it soon becomes small and feeble. Buboes may occur in any situation, but they are most common in the groin, axilla and neck. Pain and tenderness in the infected nodes are sometimes noted at the onset, and often precede the tumefaction. The surrounding tissues are usually edematous and the overlying skin may be somewhat reddened. Suppuration of the buboes, sometimes with formation of deep sloughs, is very common. More or less extensive patches of gangrene may also appear on the buttocks, abdomen, limbs, face or other parts (cellulocutaneous type). In many epidemics cutaneous ecchymoses or petechiæ—so-called "death-tokens"—and hemorrhages from the mucous membranes are of common occurrence.

As the disease advances cerebration becomes more and more impaired, mental apathy often giving way to delirium, and this in turn to a typhoid state with stupor, and eventually coma. The bowels are usually consti-

pated, the urine throughout is scanty and often albuminous, and nearly always there is a well-marked polymorphonuclear leucocytosis. Secondary pneumonia not rarely develops. Keratitis and furunculosis are occasional complications. In fatal cases death occurs as a rule between the third and fifth days, the usual cause being gradual heart failure.

*Septicemic Plague.*—This form may exist from the onset or it may be a terminal stage of the bubonic or pneumonic type. Primary cases depend upon an early and overwhelming invasion of the blood stream with plague bacilli. The systemic depression is profound and death often occurs within 2 or 3 days, in some cases (pestis siderans) before the appearance of either buboes or pneumonia. A positive diagnosis can be made only by finding the bacilli in the blood.

*Pneumonic Plague.*—Primary pneumonic plague is much less common than the bubonic form, in most epidemics not more than 3 or 4 per cent. of the cases being of this type. In the great Manchurian outbreak of 1910–11, however, the majority of cases were pneumonic (Strong and Teague[1]). In this form the disease is highly contagious and is transmitted from person to person by droplets of sputum expelled in coughing. The systemic disturbance does not differ from that observed in the more severe cases of bubonic plague, but the condition of the lungs is an early and conspicuous feature. The pulmonary symptoms correspond more or less closely to those of ordinary pneumonia, although in many instances the sputum is thin and serosanguineous and the physical signs are ill-defined. Recovery rarely, if ever, occurs.

*Ambulatory Plague (Pestis Minor).*—In this form there is usually swelling and tenderness of one or more lymph-nodes, but the constitutional disturbance is so mild that it causes scarcely any inconvenience. Occasionally, however, suppuration takes place, and for this the patient may seek relief. Ambulatory plague is especially dangerous to the community as it may be readily overlooked or concealed.

**Diagnosis.**—Once the presence of plague is suspected from the clinical findings, the diagnosis can usually be made certain by the identification of plague bacilli in smears from material aspirated from buboes or, in case of suspected pneumonic plague, in smears from the sputum. In many cases, however, an absolute diagnosis must depend upon blood-cultures and animal inoculations.

**Prognosis.**—The mortality of the bubonic form varies considerably in different epidemics, but the average is about 75 per cent. In the East it is usually much higher among the natives than among Europeans. The pneumonic and septicemic types are almost invariably fatal.

**Prophylaxis and Treatment.**—Important safeguards against the spread of plague are isolation of the sick and proper disposal of the dead; rigid quarantine, thorough disinfection of the patient's discharges, and all articles that may have become soiled with the discharges; and good general sanitation, including the prevention of overcrowding, the proper disposal of excreta and garbage, and especially the destruction of rats and their haunts. Haffkine's vaccine of heat-killed bacilli should also be used, as it seems to afford some protection, at least in the bubonic form of the disease. The immunity, however, usually lasts but a few weeks. Attendants should wear close-fitting undergarments and puttees to protect them from the bites of fleas and, in the case of pneumonic plague, masks of gauze provided with celluloid goggles.

The treatment of plague apart from the use of antitoxic serum consists

[1] Philippine Jour. of Sci., 1912, vii.

chiefly in the maintenance of strength by rest and judicious stimulation with strychnin, digitalis, etc., in the control of fever by cold sponging, and in the procuring of sleep and relief from general distress by the use of morphin and bromids. The buboes should be treated on surgical principles. Yersin's antiplague serum seems to have been an aid to recovery in some epidemics. It should be given in large doses, from 100 to 200 mils, and preferably intravenously.

## LEPROSY

(Lepra; Elephantiasis Græcorum)

**Definition.**—Leprosy is a specific, infectious disease, of extreme chronicity, caused by *Bacillus leprœ*, and characterized by granulomatous infiltrations resembling those of tuberculosis and syphilis and involving the skin, the mucous membranes, particularly those of the nose and throat, the peripheral nerves, and to a less extent the viscera.

**Etiology.**—Leprosy is known to have prevailed in India and Egypt many centuries before the Christian era. In the Bible the term leprosy is probably used to designate a number of different affections. Introduced into Europe in the days of Pompey, the disease was widely spread by the crusaders and in the 14th century it was so prevalent, that thousands of asylums (leprosaria) were required for the care of its victims. In the 15th century, however, as a result of strict segregation, it seems to have almost entirely disappeared. At present there are a considerable number of cases in Norway and Sweden, in the Balkan region, and in parts of France and Spain. Japan, the Philippines, China and India are heavily infected, and this is true also of certain parts of Africa. In the United States the chief foci are in Louisiana, Florida, and Minnesota, although there are a number of lepers in many of the other states. Only a few cases, however, have been observed in native-born Americans. The disease is found also in Hawaii, New Caledonia, New Zealand, Australia, and the Central and South American States.

Leprosy is but feebly contagious, being transmitted from one person to another only after prolonged and very intimate contact. Physicians, nurses and other attendants upon the sick only rarely contract it. Children frequently acquire the disease through contact with their leprous parents, but there is no evidence that heredity has any etiologic influence. Males are affected about twice as frequently as females. Crowding and filth favor its spread.

The exciting cause of leprosy is *Bacillus leprœ*, discovered by Hansen in 1874 and found in the specific lesions and in the discharges therefrom, being often present in large numbers in the secretions of the nose and mouth when these parts are affected. The organism is acid-fast and resembles the tubercle bacillus, although it stains more solidly, decolorizes somewhat more readily, and is usually present in much greater numbers. It is cultivated with great difficulty, and unlike the tubercle bacillus, is not pathogenic for the lower animals. Rat leprosy appears to be an independent affection and not communicable to man. The mode by which leprosy is transmitted still remains obscure. Whether the organism enters the body through wounds or abrasions by direct inoculation, through the nasal mucosa or upper respiratory tract by inhalation, through the alimentary canal in contaminated food, or through the genitals during sexual intercourse

is not known. There has been a suspicion, but no proof, that bed-bugs, fleas or itch mites may be concerned in the transmission. It is believed that the degree of contagiousness lessens with the duration of the disease (Campana, Dyer).

**Morbid Anatomy.**—There are two chief varieties of the disease. One in which the granulomatous infiltrations affect especially the skin and mucous membranes—*nodular leprosy*, and one in which the lesions are confined principally to the peripheral nerves—*anesthetic leprosy*. In many cases, however, both forms are associated, constituting what is known as *mixed leprosy*.

Nodular leprosy is characterized by the appearance of nodular formations, varying in size from a pea to a walnut, and diffuse fibrous infiltrations in the skin and mucous membranes. The face is usually the part first affected. Of the mucous membranes, those of the nose, mouth, throat, larynx and eyes are chiefly involved. Characteristic leprous foci, usually microscopic (miliary lepromata), may also be found in the viscera, especially the liver and spleen. The lymph-nodes in the regions of the leprous nodules are, as a rule, enlarged. Unless injured, the cutaneous nodules resist ulceration for a long time, often for many years. When ulceration does occur it frequently leads to extensive destruction of tissue, scarring, and deformity (lepra mutilans). Microscopically, the leprous infiltration, which begins in the corium and about the bloodvessels, is made up chiefly of new mononuclear cells, some of which are extremely large, pale, vacuolated phagocytes (lepra cells), loaded with bacilli. Giant cells may also be seen. The walls of the bloodvessels are thickened. Evidences of caseation are wanting. The bacilli are found not only in the so-called lepra cells, but also free in the lymph-spaces and in phagocytic cells in the bloodvessels.

In anesthetic or neural leprosy the granulation tissue, which apparently springs from the perineurium, causes nodular and fusiform swelling of the nerves and ultimately, as a result of compression, degeneration of their axis-cylinders. With destruction of the nerve-fibers come various sensory disturbances, especially anesthesia, bulbous eruptions, perforating ulcers, muscular palsies and atrophies, contractures, absorption of the bones of the hands and feet, dropping off of the fingers and toes, etc.

**Symptoms.**—The period of incubation varies from a few weeks to many years. As a rule, it is from 3 to 5 years. Months before any objective signs appear the patient may complain of malaise, headache, vague pains, paresthesiæ, weariness, and mental hebetude. The first definite indication is usually a succession of sharply defined erythematous patches, which are bright red, soon changing to reddish-brown, and which are particularly prone to appear on the face, forearms and backs of the hands. At first these patches, some of which may be infiltrated, are hyperesthetic, but later they become anesthetic and sometimes lose their pigmentation. Pale vitiligo-like areas, with or without pigmented borders, may appear simultaneously. It is characteristic of leprous macules to remain dry even when there is general perspiration. Infiltrations into the lobes of the ears, the nose or other parts may also be an early feature. With each outbreak of macules attacks of irregular fever usually occur. Sooner or later the disease takes on the characteristics of one of the two well-recognized types.

*Nodular Leprosy.*—This form is characterized by the development months or years after the first macules have appeared of distinct subcutaneous nodules of a reddish-brown color, painless and elastic to the touch. These usually appear on the sites of the macules and as a rule are most extensive on the face. The scalp is rarely, if ever, attacked. Aside from the nodular

elevations, the forehead is deeply furrowed, the lobes of the ears, the brows, and the lips are thickened, and the nose is broadened, the face in consequence acquiring a leonine appearance. The hair of the outer half of the eyebrows and the eye-lashes often fall out. The nodules may remain indefinitely without change, they may slowly disappear by absorption leaving areas of pigmentation or cicatricial atrophy, or they may undergo ulceration, especially upon slight injury, and cause various mutilations. Infiltration in the nose leading to ulceration of the septum and discharge is a common and often an early feature. Involvements of the larynx, causing a husky raucous voice, and of the eyes resulting in distortions of the lids, blindness, ulceration, and finally in painful shrunken globes, requiring enucleation, are also common. The patient's general health may remain fairly good for a long period, although there is often evidence of both mental and physical depression. Paroxysms of fever, accompanied by an evanescent papular exanthema, sometimes occur. They have been ascribed to the breaking down of the leprous lesions and the liberation of an excess of toxins (Dyer). Ultimately cachexia supervenes. Pulmonary tuberculosis and chronic nephritis are not uncommon sequels. The bacilli may occasionally be found in the blood, and in a large proportion of cases the Wassermann reaction is positive even in the absence of syphilis. The luetin reaction, however, is negative.

*Anesthetic Leprosy.*—In this type the prodromal symptoms are frequently so mild that they escape observation. Lancinating pains along the nerves of the extremities, however, sometimes occur. The macules are usually the same as those of nodular leprosy, except that they show less preference for the face and occur with greater frequency. With chronicity they also display a marked tendency to clear in the center, to spread peripherally, and to coalesce, forming gyrated figures. Although usually hyperesthetic at first, they soon become anesthetic. Anesthesia in areas supplied by the affected nerves, most frequently the ulnar, median, peroneal, and facial, is an early and characteristic phenomenon. In some instances the nerve trunks themselves are palpably enlarged and tender. As the disease advances muscular palsies, atrophies and contractures supervene. One of the earliest contractures is crooking of the little finger. With extensive nerve degeneration the hands assume a claw-like (main-en-griffe) character, or the fingers and toes and successive portions of the limbs slowly disappear, often without ulceration, as the result of bone absorption and atrophy. Perforating ulcers of the feet, similar to those of tabes, are fairly common, and occasionally bullous eruptions are observed. Corneal ulceration and ectropion, due chiefly to paralysis of the facial muscles, occurs in many cases.

**Diagnosis.**—The diagnosis is often difficult, especially in the early stages. It is based upon the peculiar macular eruption, the presence of pallid atrophic patches which show loss of sensation and absence of sweating, painless, pigmented nodular formations, discrete areas of anesthesia, thickening of the ears and nose, irregular enlargement of the nerve-trunks and above all upon the detection of lepra bacilli in the nasal mucus or scrapings from nasal ulcers or in material obtained from incised nodules or spots. While usually difficult to demonstrate in the spots the bacilli are easily found, as a rule, in the nodules and in scrapings from the nose.

The resemblance of *syringomyelia* to anesthetic leprosy is at times very close. In syringomyelia, however, the atrophic changes are almost always limited to the upper extremities and the anesthesia is usually radicular in type. Further, spastic phenomena in the legs, pronounced increase of the tendon reflexes, disturbances of the bladder and rectum, nystagmus, bulbar symptoms and muscular atrophy of the humero-scapular type point to

syringomyelia; while a history of preceding macular eruptions, the presence of oval, white anesthetic spots, perforating ulcers, upper facial paresis, ectropion and atrophic osteoporotic changes in the bones, as shown by x-rays, point strongly to leprosy.

**Prognosis.**—The outlook for cure is unfavorable, although the progress of the disease is slow and remissions lasting months or years are not uncommon. In some cases the disease has been completely arrested. The duration of anesthetic leprosy is usually longer than that of the nodular type and may exceed 20 or even 30 years.

**Treatment.**—Segregation offers the only hope at present of eradicating the disease. In this country, owing to the lack of uniformity in the laws of the various states, the establishment of a national leprosarium is much to be desired. With the disease under federal control, patients with pure anesthetic leprosy, who are probably not a menace to the community, might as in Hawaii, be paroled and required to report to a government physician once in every 3 or 4 months.

As to treatment, it is universally admitted that a salubrious climate, wholesome food and good hygienic surroundings influence all cases favorably. Hot baths at frequent intervals are undoubtedly of value. Tonics, especially strychnin, arsenic and iron, are usually indicated. Some writers believe that in the early stages the disease can be arrested by excising the first lesions and cauterizing their bases. Of the many special remedies chaulmoogra oil alone has stood the test of time. It is given in capsules in doses of 5 to 10 minims (0.3–0.6 mil), gradually increased, according to tolerance, to 1 or 2 drams (4.0–8.0 mils), three times a day. Because of its nauseating effects the oil is often given subcutaneously. In the Philippines, Heiser had very good results from the hypodermic use of a mixture of 60 mils each of chaulmoogra oil and camphorated oil with 4 grams of resorcin. The injections were made weekly, the dose being gradually increased from 1 mil to the point of tolerance. McDonald and Dean,[1] of Honolulu, have recently reported favorably upon the use of the ethyl esters of chaulmoogric and hydonocarpic acids (constituents of chaulmoogra oil) by intramuscular injection, but the preparations are not yet commercially available. Surgical treatment, as amputation of hopelessly ulcerated fingers and toes, tracheotomy for laryngeal stenosis, nerve stretching for perforating ulcers, etc., is not rarely required.

[1] Jour. Amer. Med. Assoc., Nov. 27, 1920 and May 28, 1921.

# INFECTIONS DUE TO PROTOZOA

## SYPHILIS

(Lues Venerea; Pox)

**Definition.**—Syphilis is a chronic infectious disease, caused by the *Spirochæta pallida*, communicated from one individual to another by direct contact with the specific lesions or their secretions, or transmitted by infected parents to their offspring during gestation, and characterized by a general septicemia with a great variety of local lesions, many of which are due to a concentration of the spirochætæ in the parts affected.

**History.**—The origin of syphilis, like that of many other diseases, is not known. Although the malady seems to have existed from prehistoric times, it did not attract public attention until the latter part of the fifteenth century, when it assumed epidemic prevalence. The view first put forward by Freind in his *History of Physic* and accepted by many investigators that syphilis originated in America and was imported to Europe by the sailors of Columbus does not rest on very strong evidence. All authorities are agreed, however, that the great epidemic of the fifteenth century can be traced to the campaign of Charles VIII, of France, and the scattering of his troops after the breaking up of his army in 1495.

The name syphilis ($ovs - \phi\iota\lambda os$–swine lover, or, possibly, $\sigma\iota\phi\lambda\acute{o}s$—maimed or impotent) originated with the Veronese poet-physician, Fracastoro (1483–1553), who made the disease the subject of a poem, in which the hero, a shepherd and Syphilis by name, is charged with bringing the curse of the infection upon the earth by blaspheming the Sun God. It was not until about the middle of the nineteenth century that syphilis, gonorrhea, and chancroid were clearly distinguished from one another. Even the astute John Hunter taught that the matter of gonorrhea could produce syphilis. Ricord (1838) was the first to establish definitely the identity of gonorrhea and to his pupil Bassereau belongs the credit of proving that chancroid is a separate disease from syphilis. A new era in the experimental research in syphilis began with the successful transmission of the disease to apes by Metschnikoff and Roux[1] in 1903. Two years later Schaudinn and Hoffmann[2] announced the discovery of the spirochæta pallida, since conceded to be the etiologic agent of the disease, and in 1906 Wassermann, Neisser and Bruck[3] devised the method of serum diagnosis with which we associate their names and which is based upon the principle of complement fixation discovered in 1901 by Bordet and Gengou.

Accurate knowledge of visceral syphilis dates from the studies of Dittrich (1849) and Wilks[4] (1862). Although Ambrose Paré, Morgagni and other early masters recognized that syphilis played an important rôle in the etiology of arterial disease, we owe especially to Heiberg (1877), Heller, and Doehle[5] our present understanding of the peculiar features of syphilitic aortitis and the relation of this condition to aneurysm. As early as 1857

[1] Ann. de l'Inst. Pasteur, 1903, 1904, 1905, 1906, 1907.
[2] Arb. a. d. Kais. Gesundheitsamt, 1905, xxii.
[3] Deutsch. med. Woch., 1906, xxxii.
[4] Trans. Path. Soc., 1862, vol. viii.
[5] For literature see the paper of Ophuls, Amer. Jour. Med. Sci., 1906, cxxxi.

Esmarch and Jessen drew attention to the fact that paretic dementia occurs especially in persons who have had syphilis, but it was Fournier who first expressed the opinion that both paretic dementia and tabes dorsalis are essentially syphilitic processes.

Mercury, originally introduced into therapeutics by the Arabs, came into general use as an antisyphilitic remedy in the fifteenth century, about the time of the great epidemic. Wallace of Dublin (1836) was probably the first to employ potassium iodide in the treatment of the disease. Arsenic compounds were first used against syphilis in 1905 and four years later Ehrlich introduced the hydrochlorid of di-oxy-diamido-arsenobenzol (arsphenamin) as a parasitotropic remedy.

**Etiology.**—Syphilis is prevalent throughout the world. No age is exempt and the two sexes are about equally affected. Natural immunity is rarely, if ever, observed, although some persons seem to be more susceptible to it than others. While as widespread as ever, the disease, on the whole, appears to be less virulent in its expressions than formerly. About 20 per cent. of all hospital patients and at least 10 per cent. of the entire population give evidence of infection. It is essentially a disease of mankind, although experimentally it can be transmitted to certain lower animals, such as anthropoid apes and the rabbit. Infection is transmitted directly or indirectly from one person to another by inoculation of the specific parasite (*acquired syphilis*) or is communicated from parent to offspring during gestation (*congenital syphilis*).

The specific cause of syphilis is the *Spirochæta pallida* (Treponema pallidum) which is more closely related to the protozoa than to the bacteria. This organism may be found in all the lesions of every stage of the disease, and also in the lymph-nodes, in the blood, and in the cerebrospinal fluid. It is especially abundant in the acute lesions of the acquired form and in the tissues generally of the syphilitic fetus. As seen with the dark-ground illuminator it is a delicate, very slightly refractile thread, closely wound in the form of a spiral, which is from 6 to 20 microns long (1 to 3 times the diameter of a red blood cell), pointed at the ends, and provided with flagellæ. Its movements are screw-like, lateral and to-and-fro, the last two being much less rapid than those of the non-pathogenic spirochetes. It stains pale red with Giemsa's fluid, while the coarser, highly refractile *Spirochæta refringens*, with which it is often associated, stains dark purple. Culturally, the organism shows strict anaërobiosis, requires fresh sterile animal tissue and serum in the media, and does not produce coagulation or a putrefactive odor. Syphilis has been passed indefinitely from ape to ape and both apes and rabbits have been successfully inoculated with the blood, the cerebrospinal fluid and the semen of patients in the early stages of the disease.

In acquired syphilis infection takes place, as a rule, during sexual intercourse or perversions thereof, although it not rarely occurs aside from sexual acts (*syphilis insontium*), being transmitted through abrasions of the skin, as of the hands of physicians and nurses who are in attendance upon syphilitic patients, by way of the lips in kissing, or indirectly by means of infected drinking vessels, pipes, razors, tattooing instruments, etc. Fortunately, the parasite does not remain alive for more than a few hours outside of the animal body, otherwise the danger of mediate infection would be much greater than it actually is.

It was formerly believed that one attack of syphilis afforded protection against another, but it is now generally recognized that the resistance which is shown by victims of the disease to reinfection depends upon the activity of the first infection, which has not been completely destroyed by treatment,

although it may have been rendered entirely quiescent. With actual cure susceptibility to reinfection returns, and therefore the disease does not confer immunity in the ordinary sense of the term, which implies a refractory state incompatible with the life of the infectious agent. Even the existence of syphilis may not invariably afford absolute protection against a new infection, a second inoculation with a sufficiently large quantity of active virus rarely resulting in lesions corresponding more or less closely with those of the stage of disease in which the patient is at the time (superinfection). Generally speaking, the degree of contagiousness of syphilis decreases with the time elapsing after infection has occurred, moreover, the late lesions of the disease, although distinctly infectious, afford much less opportunity for the spread of the contagium than those of the early stages, as unlike the latter, they are not usually situated on the genitals or in the mouth.

*Congenital syphilis* is not a matter of inheritance, in the true sense of the term, but of intra-uterine infection. It may be acquired directly from the mother, the father being healthy, or it may be acquired from the mother, who has been infected by the father. Formerly it was thought that paternal infection of the fetus might occur directly by way of the ovum, with secondary or passive immunization of the mother, as has been assumed from the original statement of Colles' law,[1] which in effect is that apparently healthy women bearing syphilitic children do not contract syphilis when exposed to infection. By means of the complement-fixation test, however, it has been found that such apparently healthy mothers are refractory to the disease, not because they have acquired immunity, but because they really have syphilis in a latent form, the hemolysis-inhibiting substance being produced only in the presence of spirochetes. Similarly, Profeta's law that apparently healthy children of syphilitic mothers cannot acquire syphilis from outside sources is explained by the fact that infection is already installed, although it is without active clinical signs. Children in such cases almost always yield, sooner or later, a positive Wassermann reaction. Therefore, barring the exceptional cases in which the fetus acquires the disease at birth from early vaginal lesions, it seems likely that congenital syphilis is always transmitted through the syphilized mother by way of the placenta, and that direct infection of the embryo by the father never occurs. As a rule, the older the syphilis in the parent, the less likelihood there is for infection of the child. Fresh syphilis, especially in the mother, generally results in early death of the fetus. Habitual abortions are due to syphilis in many cases, and the usual time for interruption of the pregnancy is after the fourth month, when the placenta is fully developed. As the strain of the virus in the parent becomes attenuated, living children with active or with latent syphilis may be born.

As congenital syphilis may remain latent until adult life, and as the late lesions of the disease are now known to be due to renewed activity of the spirochætæ, there seems to be no reason why syphilis should not occasionally be transmitted to the third generation. The question, however, is beset with difficulties as it involves the proof of the sexual purity of two persons up to the time of maturity.

**Pathogenesis and Pathology.**—When a successful inoculation has been effected the spirochætæ multiply in the lymph spaces at the point of entry, and after *a period of incubation*, varying from 2 to 6 weeks, give rise to a localized cellular infiltration composed of densely packed lymphocytes, plasma cells and large mononuclear cells. These elements are especially conspicuous

[1] For Colles' original statement, which was made in 1837, see *The Works of Abraham Colles*, New Sydenham Soc., London, 1881, Chap. XIII.

about the bloodvessels, the walls of which are enormously thickened. Over the cellular accumulation there is some epithelial proliferation which is often eroded. Thus constituted the primary lesion assumes the form of a small, sharply defined hyperemic area or red papule which is known as the chancre. With erosion of the epithelial covering the hyperemic area or papule is transformed into a shallow ulcer, usually with a red (beefy) indurated base. This ulcer may, of course, become secondarily infected with pyogenic cocci. In a short time the spirochætæ reach the regional lymph-nodes, where they multiply and eventually set up a simple (non-suppurative) adenitis. The latter usually shows itself a few days after the appearance of the chancre. Further dissemination of the organism occurs by way of the general lymph stream, with the production of polyadenitis, and thence by way of the thoracic duct and circulating blood. Recent researches indicate that the spirochætæ are widely distributed over the body even before the primary lesion can be detected.[1] When the concentration of organisms in the blood has become sufficiently pronounced, secondary lesions of the skin and mucosæ make their appearance, with fever, muscular pains etc. The interval between the development of the chancre and the onset of this *secondary period* is usually from 6 to 8 weeks. The secondary lesions are not microscopically distinctive. As a rule, they present a circumscribed cellular infiltration, which is especially marked about the bloodvessels and which is composed chiefly of lymphocytes and plasma cells, with an occasional fibroblast. Especially conspicuous among the secondary lesions and also important as ready sources of infection, are the so-called mucous patches and the similar flat condylomata. In both of these lesions there is extensive infiltration of the papillæ with proliferation and maceration of the overlying epithelium. The mucous patches may be found on the mucosa of the mouth, throat, vagina or anus, and appear as flat elevations of a grayish color and covered with slimy exudation. The condylomata are usually found where two skin surfaces are in apposition, appearing as small lobular elevations, somewhat flattened and often more or less macerated by heat and moisture. The lesions of the secondary period are, as a rule relatively benign and heal without serious injury to the tissues.

In many cases the period of secondary symptoms, which lasts from 2 months to a year, is followed after a variable interval of latency (a few weeks to many years) by a *period of tertiary symptoms*, the duration of which is indefinite. Recent studies have shown that in the majority of cases the latency is merely clinical and that in the interval between the secondary and the tertiary manifestations not only spirochætæ but also active lesions are to be found in certain parts, especially the aorta, heart, testes, adrenals, central nervous system, liver, or spleen. Generally speaking, the tertiary lesions are more localized and more destructive than those of the secondary period, and, if they heal, are more likely to be followed by cicatricial deformity, although it must be admitted that it is not possible to draw sharp lines of demarcation between the periods of syphilis; indeed, in some cases the so-called tertiary manifestations develop very early, even before the chancre has healed, and in others, recrudescences of the so-called secondary symptoms occur many years after the original infection.

The most characteristic lesion of the tertiary period is a tumor-like mass of granulation tissue, which, from its elastic consistency when old, is known as the gumma. This mass varies from a size so small as hardly to be visible to that of an orange or larger. When recent it is grayish-red, soft and gelatinous, but when old, yellowish-white, firm and elastic, these changes being

[1] Brown and Pearce, Arch. Dermat. and Syph., Oct., 1920.

analogous to those occurring in tubercles. Histologically, the gumma is composed of epitheliod cells, mingled with lymphocytes and plasma cells and a few giant cells. As the lesion ages it tends to heal, the usual procedure being gradual softening and absorption of the mass, with the formation of cicatricial tissue, the contraction of which produces a deep radiating scar. A gumma may usually be distinguished from a tubercle by the history, the location of the lesion, the bacteriologic findings, the occurrence of new capillaries within the tumor mass, and the tendency of the latter to become surrounded by a dense capsule and to undergo fibrous metamorphosis with healing. Gummata are found in the periosteum and bones, in the liver, brain, lungs and other organs, in the subcutaneous and submucous tissues, and in the walls of bloodvessels.

In very many instances of tertiary syphilis the reaction to the presence of the spirochætæ does not result in the development of distinct gummatous tumors or nodules, but takes the form of a diffuse infiltration of the tissues, particularly the stroma about the bloodvessels and lymphatics, with plasma cells and lymphocytes. This process is common in the heart, aorta, nervous system, pancreas and testes. It usually ends in patches of atrophy and destruction of the parenchyma, fibrosis, and scarring.

In explanation of the fact that in the tertiary stage, when resistance to infection from without is highly developed, the lesions often show great tissue destruction. Levaditi[1] suggests that the resistance developed during the primary stage may be sufficient to hold the parasites in check for a time until they acquire a certain degree of immunity of their own to the antibodies of the host when they produce the characteristic phenomena of the secondary stage. In the reaction to the infection of this stage greater quantities of antibodies are formed, which suppress the growth of the parasites to a large degree, although not destroying all of them. In the course of time the tissues themselves, however, may develop a condition of hypersensitiveness, so that even a few spirochætæ may be able to cause extensive local necrosis.

Formerly certain affections of the central nervous system, which were known to be of syphilitic origin, more particularly general paresis and tabes dorsalis, were regarded as *parasyphilitic manifestations* and assumed to be due to a toxin only indirectly connected with syphilis. This view was entertained because the primary and secondary symptoms are, as a rule, insignificant in patients who are destined to develop either general paresis or tabes, because these diseases are peculiarly intractable to antisyphilitic treatment, and because the lesions characterizing them are of a degenerative rather than of a proliferative type. In both of these affections, however, the spirochætæ have been demonstrated in the tissues and it is now generally recognized that so-called parasyphilitic conditions are in reality manifestations of active syphilis.

Soon after the spirochætæ have become generalized (usually in from 10 to 30 days after the appearance of the chancre or in from 4 to 8 weeks after inoculation) a bio-chemical reaction occurs in the blood and body-fluids of the syphilitic patient resulting in the formation of antibodies belonging to the group known as antilipoids. These react in such a way with corresponding lipoids that if complement be present at the time, this is fixed, and upon the subsequent addition of washed red corpuscles and a suitable hemolytic amboceptor to the mixture of lipoid, antilipoid and complement, hemolysis does not occur or is more or less impeded. This phenomenon is the basis of the *Wassermann test* for syphilis. The hypersusceptibility of the

[1] Ztsch. immunitäsforsch. Referate, 1910, ii, 277.

syphilitic subject to the corresponding antigen also has been utilized for diagnostic purposes. Thus, by introducing a small amount of a devitalized culture of spirochætæ pallida into the skin of the patient an allergic reaction is produced comparable to that of von Pirquet in tuberculosis (Noguchi's luetin test).

**Symptoms.**—The earliest indication of syphilis is the so-called *chancre*. This appears at the site of inoculation, which is usually on the prepuce, sulcus or glans penis in males and on the vulva, vagina, or cervix of the uterus in females. In some cases it is extragenital, the parts most frequently affected being the lips, fingers, nipples, cheeks, tongue and tonsils. As a rule, the chancre takes the form of a minute, sharply circumscribed hyperemic area, which soon becomes a superficial abrasion, or of a minute, hard, dusky red papule, which in a very short time presents a shallow ulcer at its summit. From the ulcer there issues a considerable amount of thin, watery secretion, which may dry and form a scab. Many departures from these characteristics, however, are observed. In some cases the primary lesion is so small and is accompanied by so little inflammatory reaction that it fails to attract the patient's attention. In other cases it is clinically indistinguishable from the soft sore (chancroid), although it harbors the parasite of syphilis. Multiple chancres, the result of simultaneous or successive infections, are not uncommon. If there is no secondary infection by pyogenic organisms, healing of the primary sore usually takes place within a few weeks, but slight cicatricial induration often remains for a long time.

Within a few days of the appearance of the chancre the regional lymph-nodes, which in most cases are the inguinal nodes, become enlarged and indurated, forming so-called *indolent buboes*, and in the course of 2 or 3 weeks the lymph-nodes throughout the body undergo similar changes.

Within from 6 to 8 weeks after the occurrence of the chancre, that is, within the course of 2 or 3 months after inoculation, the *secondary manifestations* indicative of a general infection make their appearance. In most cases these secondary manifestations consist of constitutional disturbances of varying degrees of intensity, but as a rule, comparatively mild, and certain affections of the skin and mucous membranes. Fever is not uncommon. Usually it is slight (100°–101° F.), but sometimes it is high (103° F. or more), and it may be remittent or, rarely, intermittent and accompanied by chills. Not infrequently it has been mistaken for that of typhoid fever, rheumatism, tuberculosis, or malaria. Other evidences of a general infection are often seen in malaise, anorexia, headache and backache, pains in the bones, especially at night, sore throat, slight enlargement of the spleen, anemia and lymphocytosis.

The cutaneous disturbance takes the form of a macular, papular or pustular eruption (cutaneous syphilides). Whatever its nature, the eruption is, as a rule, generalized, more or less symmetrical in distribution, superficial, free from itching and with a tendency to acquire a coppery pigmentation (ham-colored) on fading. Especially significant is the simultaneous appearance of several types of lesions (polymorphism). Although the rash is usually more or less general, it commonly shows a predilection for the forehead near the margin of the hair, the palms of the hands and soles of the feet, and the region about the genitals. The commonest and earliest eruption is the roseola or macular syphiloderm, which consists of rounded or irregular, slightly raised erythematous spots, varying from 5 to 10 mm. in diameter. It lasts from 1 to 3 weeks or longer and frequently recurs. The papular syphilide may accompany or follow the macular rash. The papules are usually abundant and widespread, and vary in size from a pinhead to a

bean. A papulo-squamous eruption is not uncommon. It resembles psoriasis, but may be distinguished by its predilection for the palms and soles, the relatively slight scaling and the grayish or dirty-gray color of the scales. The pustular syphilide, according to the size and course of the lesions, may resemble acne, variola, impetigo or ecthyma. Upon opposing skin surfaces, such as the perineum, nates, genitalia, axillæ, etc., flat moist papules or wart-like formations often make their appearance. Similarly, upon the mucous membranes of the mouth, throat, vagina, anus, etc., so-called mucous patches—moist, grayish tabular elevations, with a tendency to ulceration—are frequently found. On the fauces or palate these patches sometimes coalesce and form superficial serpiginous or "snail-track" ulcers.

Concurrently with the roseola the hair may become dry and lustreless and fall out; the nails also may become brittle and deformed, and occasionally there is paronychia. The pains in the bones and joints are not usually accompanied by objective changes, but sometimes there is obvious periostitis or hydrarthrosis. Any part of the eye may be affected, but early syphilis shows a predilection for the iris and choroid. Nearly one-half of all cases of iritis are due to syphilis. Deafness, due to changes in the eighth nerve or in the labyrinth, is occasionally observed.

Lesions of the central nervous system, bloodvessels and viscera are usually late features of the disease although it must be recognized that after the primary stage the manifestations often appear very irregularly. Indeed, infection of the central nervous system occurs in a large proportion of cases of early syphilis, but as a rule it dies out before any damage ensues or it remains latent only to become active after a period of years. Exceptionally, however, meningitis occurs very early, even before the primary sore has healed, and rarely syphilitic encephalitis or myelitis displays its initial symptoms during the first month of the disease. Serious damage to the cardiovascular system may also occur during what is often called the florid stage of syphilis and occasionally acute nephritis is an early manifestation. Jaundice has not infrequently been noted at the time of the exanthem, and in about 10 per cent. of the cases it has been followed by the usual evidences of acute yellow atrophy. In 1911 Umber[1] collected reports of 50 cases of syphilitic icterus gravis. After the stage of secondary symptoms, which lasts from two months to a year or more, the patient may possibly remain henceforward in good health. More frequently, however, after the lapse of a variable period, usually two or three years, but sometimes twenty years or more, lesions of the so-called *tertiary stage* manifest themselves. Although a distinct interval between the secondary and tertiary stages is the rule, cases are sometimes observed in which the symptoms of the one stage pass without break into those of the other or become intermingled. The characteristic lesions of the tertiary period are the gummata, which may form in the skin, mucous membranes, muscles, bones or viscera. The small gummata of the skin produce the nodular (tubercular) syphilide, which consists of firm, deeply-seated, smooth or slightly scaly papules, of a yellowish red or coppery color, and usually of the size of small or large peas. As a rule, the papules are few in number, show a marked tendency to occur in groups, forming segments of circles or serpiginous tracts, are sluggish in their course, and terminate in ulceration. The larger gummata of the skin appear as more or less circumscribed painless tumors, which grow slowly or rapidly, and tend to break down forming deep, punched-out, kidney-shaped ulcers.

Gummata of mucous membranes occur as small nodular masses, gradually increasing in size and resulting in extensive ulceration, with permanent

[1] Münch. med. Woch., 1911, 58.

loss of tissue, and healing with deforming scars. Such gummata are most common in the mouth, pharynx, rectum and larynx. The bones are a favorite seat of tertiary lesions, the cranial bones, tibia, clavicle and sternum in particular being frequently affected. Superficial gummata appear as hard painless nodes, which often break down, causing ulceration of the superficial parts and extensive necrosis of the bone itself. Surrounding the dead area there is commonly a wall of rough osteophytes, which is somewhat characteristic of syphilis as contrasted with tuberculosis. The joints and bursæ are sometimes affected in a similar way. Clinically, the arthropathies of late syphilis may resemble either tuberculosis of the joints or arthritis deformans. Their recognition must depend largely upon associated data. Syphilitic spondylitis has been frequently described. In more than one-half of the recorded cases the localization was in the cervical region. The condition may be mistaken for Pott's disease or for hypertrophic cervical pachymeningitis. The roentgen ray has sometimes been helpful in the differentiation. In so-called syphilitic dactylitis there is a gummatous infiltration of the phalangeal bones or joints. The syphilitic bursopathy of Verneuil, occurring especially at the elbow wrist, knee, or, ankle, is a rare manifestation.

Gummata also form in the voluntary muscles, occurring as circumscribed somewhat movable indurations, which tend to disappear by absorption. Healing may lead to more or less distortion from scar formation. Gummata and other tertiary lesions of the viscera, bloodvessels and central nervous system, owing to their great importance to the internist, are considered more fully in the sections that follow.

In addition to local manifestations, certain constitutional disturbances may also be present in late tertiary syphilis. Fever of an intermittent or remittent type, occurring for variable periods with intervals of apyrexia, is not very uncommon. It may readily be mistaken for that of tuberculosis, sepsis, or malaria, especially as it is often accompanied by chills and sweats. Again, persistent tertiary symptoms sometimes lead to marked cachexia, with emaciation and loss of strength, and occasionally amyloid degeneration of the viscera.

The effects of syphilis do not end with the ordinary tertiary manifestations. It is now recognized that certain diseases of the nervous system, such as tabes and general paresis, have their sole origin in syphilis and are the result of the direct action of the spirochæta pallida. It is remarkable also that primary, secondary, and even tertiary manifestations are, as a rule, insignificant in patients who are destined to develop grave nervous disease.

## Syphilis of the Respiratory System

Gummata and gummatous infiltration are common in the tissues of the nose, nasopharynx, pharynx and larynx. In the *nose* the bone is usually involved before the mucous membrane. Unless treatment is promptly instituted the changes result in extensive necrosis of the parts. Perforation of the nasal bones and cartilages may occur and give rise to the so-called saddle nose and a foul discharge (ozena), or there may be destruction of portions of the hard and the soft palate and of the uvula.

*Laryngeal syphilis* may show itself as a catarrhal process or as a gummatous infiltration going on to ulceration of the cartilages, with subsequent cicatrization and perhaps great distortion of the structures. The voice is husky, there is more or less cough, and if the epiglottis is involved deglutiton may be painful. Sudden edema sometimes supervenes. The condi-

tion must be distinguished from tuberculosis and carcinoma. Similar lesions may occur in the trachea or in one of the main bronchi and result in cicatricial stenosis of the canal, with hard paroxysmal cough, dyspnea with prolonged inspiration, stridor, etc. In long-standing stenosis of a main bronchus bronchiectasis and emphysema frequently develop below the site of the obstruction.

Acquired *syphilis of the lungs* is comparatively rare. It may take the form of (*a*) multiple gummata or (*b*) a fibroid process, which as a rule originates at the hilum of the lung and spreads outward along the bronchi and bloodvessels. Bronchiectasis is a common sequel. Whether a focal form of pulmonary syphilis with signs of consolidation and catarrh at an apex also occurs is uncertain, although clinical evidence indicates that such is exceptionally the case. The differentiation of pulmonary syphilis from tuberculosis of the lungs is usually difficult. In any case if the root or the base of the lung is the site of the physical signs a suspicion of syphilis should be aroused, and especially so if both the local process and the patient's general condition remain nearly stationary over a long period. Persistent absence of tubercle bacilli, the presence of syphilitic stigmata elsewhere in the body, and the results of antisyphilitic treatment are, however, the chief means of recognition. The differential diagnosis is rendered more difficult by the fact that the same individual not rarely suffers from both diseases.

In congenital syphilis the common lesion of the lungs is the so-called white pneumonia described by Virchow and which is of little more than pathologic interest. Large areas of consolidation are formed, which on section present a smooth, firm, dry surface of a grayish or yellowish white color. The chief change is a cellular infiltration into the alveoli with more or less increase in the alveolar and interlobular connective tissue. Stained sections show an enormous number of spirochætæ.

## Syphilis of the Circulatory System

Cardiovascular lesions are frequently due to syphilis. A common lesion is a distinctive type of *aortitis*—the productive mesaortitis of Doehle[1] and Heller. It is about twice as frequent in men as in women, and occurs in from 15 to 20 per cent. of all cases showing clinical evidences of syphilis. All three coats of the vessel, as well as the vasa vasorum, are involved in this condition, the changes being of a gummatous nature, comparable to those produced by syphilis elsewhere. Spirochætæ are often found in and around the affected areas. The macroscopic appearances are characteristic. The inner surface of the vessel is longitudinally wrinkled and studded with nodular elevations, some of which are grayish and translucent, while others are yellowish and opaque. The ulcers and calcareous plaques of ordinary atheroma are wanting. In the later stages the vessel is more or less thickened from reparative hyperplastic changes in the intima and shows areas of pitting and scarring. In some cases the naked eye appearances are indistinguishable from those of ordinary atherosclerosis. The arch of the aorta is the part of the vessel most often involved. The process is a chronic one, and usually a late manifestation, although recent studies have shown that infection of the aorta probably occurs in the secondary stage of syphilis, and occasionally cases are observed in which serious circulatory symptoms develop a few months after the initial sore. Dilatation of the aorta, true saccular aneurysm, and thickening and shortening of the aortic valves following downward extension of the process are important sequels of

[1] Deutsch. arch. f. klin. med., 1895, iv.

syphilitic aortitis. Indeed, most aortic aneurysms and at least 75 per cent. of all cases of pure aortic valvular disease, that is disease of the aortic valve unassociated with that of the other valves, are the result of syphilis. Rarely perforation of the aorta with fatal hemorrhage occurs in the absence of any aneurysmal dilatation. In some cases the nodular swellings are so distributed as to cause obstruction of the coronary arteries, and in rare instances even the left carotid or the innominate may be occluded. Encroachment on the lumen of the coronary arteries may result in angina pectoris or in symptoms of myocardial insufficiency. In many cases syphilitic aortitis cannot be recognized clinically before the occurrence of aortic insufficiency. Among the early symptoms and signs that are sometimes noted may be mentioned the following: Precordial pain, frequently of an anginoid character; dyspnea, occasionally paroxysmal and asthma-like; abnormal pulsation of the vessels of the neck; roughening of the first sound and accentuation of the second sound at the aortic area; dilatation of the aorta, as shown by percussion or x-ray; and a slight increase in the area of cardiac dulness.

In the smaller vessels syphilis may be manifested as minute gummata growing in the adventitia or intima. When the adventitia is chiefly affected the gummatous nodules are eccentrically located and resemble miliary tubercles, although as a rule they are somewhat larger and firmer. The lesions are especially common in the cerebral arteries and are not infrequently accompanied by gummatous meningitis. Apart from these more or less characteristic changes in the vessels, syphilis also produces directly, or indirectly through the occurrence of nephritis, a true arteriosclerosis similar to that caused by chronic intoxications of various kinds.

Syphilis plays an important part in the etiology of *chronic myocardial disease*. Occasionally the heart appears to bear the brunt of the infection. The changes are usually secondary to disease of the coronary arteries, but, as Warthin[1] has pointed out, focal areas of degeneration and interstitial proliferation may occur also as a direct result of spirochaetal activity. Circumscribed gummata of the heart are comparatively rare. The left ventricle is the part most often affected. In a number of cases heart block has occurred owing to involvement of the conducting bundle of His. Sudden death is the rule.

## Syphilis of the Genito-Urinary System

Acute syphilitic *nephritis* is relatively uncommon. It occurs in the secondary stage of the disease and usually in the first two or three months. Clinically, it resembles postscarlatinal nephritis. Death may ensue or the condition may become chronic; in many cases, however, recovery occurs after several months. In the later stages of syphilis both amyloid kidney and chronic diffuse nephritis, with more or less atrophy and destruction of the tubules and glomeruli may be observed. Gummata of the kidneys are rare. The diagnosis of renal syphilis must be based chiefly upon the evidences of syphilitic infection and the exclusion of other etiologic factors. The therapeutic test is also important, but it is not applicable, of course, in cases of amyloid disease. When syphilitic nephritis is to be distinguished from mercurial nephritis arsphenamin should replace mercury in the therapeutic test. Other features that have been regarded as more or less suggestive of renal syphilis are pronounced and persistent edema, marked albuminuria with an abundance of tube-casts of various types, and the

[1] Amer. Jour. Med. Sci., May, 1914.

presence in the urine of doubly refractile lipoid globules. The recognition of the latter requires the use of polarized light.

Syphilis of the *bladder* is comparatively rare. In the secondary period there may be small macules or multiple superficial ulcerations. In the tertiary period two types of lesions occur: gummatous ulcerations and papillomatous growths. The majority of cases have been in the tertiary period. The chief symptoms are pain in the region of the bladder, increased frequency of micturition, and hematuria, the last being the most constant. Syphilis of the *testicle* is common, both in the later stages of the acquired disease and in the congenital form. The usual lesion is a fibrous orchitis, which results in a smooth, hard, rounded, insensitive enlargement of the gland. Hydrocele of the tunica vaginalis is a frequent accompaniment. In some instances both testicles are affected. Circumscribed gummata of the testicle are occasionally observed. The affected organ is enlarged and nodular, and frequently it is adherent to the scrotal tissue. Except as an associated lesion with gummatous orchitis, syphilitic *epididymitis* is rare, although less so than was formerly believed. It is usually of the chronic indurative type and symptomless. A gummatous form, however, is sometimes observed, and rarely subacute epididymitis, with pain and tenderness, develops in the secondary stage of syphilis. Aside from chancres and the condylomata of the secondary stage, syphilitic lesions of the *female generative organs* are not often observed. Gummatous and other syphilitic changes in the vagina, uterus, ovaries and tubes have been described.

## Syphilis of the Digestive System

The primary and secondary lesions of the mouth and throat have already been mentioned. In addition, circumscribed gummata or gummatous infiltrations may appear in the lips, tongue or pharynx and give rise to considerable loss of tissue and scarring. The lesions are usually distinctive, but in some cases confusion with carcinoma or tuberculosis may occur. A smooth atrophic condition of the base of the *tongue* (indurative atrophy of Virchow) is common and significant, although it cannot be considered a pathognomonic sign of syphilis. *Leukoplakia* occurs in association with syphilis in a large proportion of cases. Gummata of the *tonsils* are rare. A few instances of ulceration of the esophagus or of stenosis as a sequel of ulceration have been described. Syphilis of the *stomach* is uncommon, although it is probably more frequent than is generally supposed. The usual finding is gummatous ulceration or diffuse syphilitic infiltration with fibrous hypertrophy of the submucosa, deformity of the organ, and perigastric adhesions. The second form sometimes simulates linitis plastica. Circumscribed gummata have also been described. The symptoms of syphilis of the stomach suggest simple gastric ulcer or, less frequently, scirrhous carcinoma. Hematemesis is comparatively rare, but anacidity or achylia is present in the majority of cases (Hausmann, Lafleur, Patella, Eusterman[1]).

Syphilis of the *intestine* is rare, except in the rectum, where gummata are common, especially in women. During the stage of ulceration, rectal gummata cause painful defecation and foul discharges; later, after healing has occurred, symptoms of stricture frequently supervene.

*Jaundice* occurs in from one-half to one per cent. of the cases of secondary syphilis and is sometimes followed by symptoms of acute yellow atrophy (see p. 177). It is probably due to invasion of the liver by spirochætæ.

[1] Amer. Jour. Med. Sci., Jan., 1917.

The *liver* is a very favorite site for tertiary syphilis. There are three types of lesions: (1) Gummata, single or multiple; (2) chronic interstitial hepatitis (syphilitic fibrosis); and (3) a combination of gummata and syphilitic fibrosis. Chronic interstitial hepatitis results from the retrogression of gummata or the organization of syphilitic granulation tissue. The liver may be merely indented with linear or stellate cicatrices, without showing much alteration in shape, or it may be coarsely lobulated by thick bands of fibrous tissue (hepar multilobatum). Sometimes one lobe is completely isolated from the other or is entirely replaced by cicatricial tissue. In other cases the appearances resemble those found in ordinary portal cirrhosis. Whether syphilis ever produces directly true portal (multilobular) cirrhosis is somewhat doubtful, although it seems to favor its occurrence. Finally, in long-standing cases, particularly those with disease of the bone, the liver may become the seat of amyloid change.

Syphilis of the liver presents a varied clinical picture. Pain and fever are the most constant symptoms, but jaundice and ascites are not uncommon. The pain may be continuous or periodic, mild or severe. The fever also may be continuous or periodic. In some cases it is very irregular and accompanied by chills and sweating, like that of septicemia, and in other cases it resembles typhoid. The liver itself is usually, but not invariably, enlarged, and may present coarse irregularities or even large smooth lobulations. According to McCrae, a striking feature is the relatively marked enlargement of the left lobe as compared with the right. In many cases the spleen also is enlarged. The disease may simulate carcinoma, abscess, septic phlebitis, chronic cholecystitis, atrophic or hypertrophic cirrhosis, or splenic anemia. In any case of hepatic disease a definite history of syphilis, a positive Wassermann reaction, evidences of syphilis elsewhere in the body, or any atypical or unusual feature in the symptom-complex should be regarded as an indication for antiluetic treatment.

Congenital syphilis of the liver may be gummatous or cirrhotic. The gummata may be miliary and multiple or large, well-formed and isolated. The cirrhotic form is the more common. It is characterized by a diffuse infiltration of young connective-tissue cells between the individual cells of the liver, forming a pericellular or monocellular cirrhosis. There are usually well-marked signs of syphilis elsewhere in the body and, as a rule, both the liver and the spleen are enlarged. Jaundice is occasionally present, but ascites is very rare. Not infrequently the infant is still-born or dies a few days after birth. In some instances the symptoms do not show themselves until the second, the third, or even the fourth decade of life, and when this is the case they do not differ materially from those of acquired syphilis of the liver.

Until recently it has been assumed that the *pancreas* is only rarely attacked in syphilis, but Warthin[1] found evidences of interstitial pancreatitis in every one of 41 cases of latent syphilis studied postmortem. He believes that his findings offer a possible explanation of the obscure etiology of many cases of diabetes. However, a positive Wassermann reaction is observed in less than 10 per cent. of the cases of diabetes.

## Syphilis of the Lymphatic System

Within a few days of the appearance of the primary sore the regional *lymph-nodes* become slightly swollen and indurated. The affected nodes are painless and, unless secondary pyogenic infection occurs, do not suppurate.

[1] Amer. Jour. Med. Sci., Aug., 1916.

By the end of the third or fourth week the lymph-nodes throughout the body become palpable and hard, and may remain so for years The change in the nodes responsible for this early tumefaction is an increase in the number of large and small mononuclear cells which fill the sinuses. In the tertiary stage of syphilis a true gummatous infiltration of the lymph-nodes in certain regions of the body is occasionally observed.

Slight swelling of the *spleen* often occurs in the secondary stage of syphilis, and if it is accompanied by headache, malaise, and fever the resemblance to typhoid may be striking. Gummata may appear in the spleen in the tertiary stage, but they are comparatively rare. Much more frequently gummatous cicatrices are found, with thickening of the capsule and enlargement and induration of the organ (chronic interstitial splenitis).

Caussade and Levi-Franckel, Anderson, Osler[1] and others have reported cases of syphilis with the clinical picture of the Banti type of splenic anemia. Marked splenomegaly is especially common in congenital syphilis. Indeed, according to Carpenter,[2] syphilis is second only to rickets as a cause of enlargement of the spleen in infancy. In long-standing cases of active syphilis the spleen, usually in association with the liver and kidneys, is likely to become the seat of amyloid degeneration.

## Syphilis of the Nervous System

Organic diseases of the nervous system rarely occur in the acute stage of syphilis, that is, during the time of the cutaneous manifestations, but in this period the nervous system is often invaded by the spirochætæ, and in consequence the cerebrospinal fluid often shows slight pathologic changes. Occasionally, however, even before the primary sore is healed, symptoms of *acute meningitis* are observed. In the later stages, usually between the fifth and the fifteenth years after infection, diseases of the nervous system are common. It has been stated that from 5 to 10 per cent. of syphilitics develop nervous lesions, but this is only conjecture, as no reliable statistics on the subject are available. Certain it is, however, that in patients who are destined to develop serious nervous disease the primary and secondary manifestations of syphilis are, as a rule, slight. Whether the important factor which determines involvement of the nervous system is infection with a special strain of spirochætæ having an neurotoxic action, or is an inherent lack of resistance in the nerve tissues themselves, or is a sensitization of these tissues by a small quantity of virus which for a time remains dormant and is later called into activity, is not known. Three kinds of *nervous lesions* may be recognized: (1) Gummata, occurring either as tumor-like masses which invade or compress the nervous tissues or as diffuse infiltrations in the meninges or about the bloodvessels of the brain or spinal cord; (2) syphilitic endarteritis, which may lead to aneurysm or rupture of the affected vessel or to thrombosis and focal softening in the brain or cord; and (3) certain parenchymatous lesions, in which the essential feature, and possibly the primary one, is degeneration or decay of special nerve tracts or nerve cells. The affections comprising the last group, which includes *tabes dorsalis*, *general paresis*, certain forms of *primary optic atrophy* and Erb's *syphilitic paraplegia*, were formerly believed to be due a toxin only indirectly connected with syphilis and were therefore referred to as parasyphilitic or metasyphilitic conditions, but it is now known that they are the direct result of the action of the spirochæta pallida and that they differ from other forms

[1] Clinical Jour., 1914, xliii, 462.
[2] Brit. Med. Jour., 1903, ii, 463.

of nervous syphilis only in presenting as the most conspicuous feature destruction of the essential nerve structures. In all forms, except in cases far advanced, a constant histologic finding is a lymphocytic and plasma-cell infiltration of the perivascular lymph spaces of the affected part.

Circumscribed *gumma of the brain* is less common than the diffuse gummatous deposit. Its favorite seat is the cortex of the cerebrum. In rare cases it may reach the size of a large walnut, but usually it is much smaller. The symptoms are those of brain tumor. Circumscribed *gumma of the spinal cord* is rare.

Syphilitic *meningo-vascular disease* is common. It frequently involves both the brain and the spinal cord, although the lesions in the latter are often insignificant in comparison with those in the former. While the brunt of the process is borne by the meninges and bloodvessels the parenchymatous tissue is always more or less involved, hence the condition is frequently referred to as meningo-encephalitis or as meningo-myelitis. Syphilitic meningo-vascular disease shows a predilection for the base of the brain, where it usually involves one or more of the cranial nerves, especially the oculomotor, the optic, the acoustic, and the abducens. The chief symptoms in order of frequency are headache, alteration in habit and disposition, insomnia, palsy of the cranial nerves and diverse motor disturbances, such as convulsions, general or unilateral, local spasms, paralytic conditions of varying extent and degree, dysarthria and aphasia. Considered individually these symptoms are not characteristic, but in their grouping, in their relation to one another, in their mode of onset and in their progress there is often a suggestion of syphilis. The phenomena are likely to be multiform, to vary in character and degree from time to time, and to appear for a time and then to disappear, only to recur again and finally to become permanent. In many cases recourse must be had to laboratory tests and to antisyphilitic treatment to establish the diagnosis. Drooping of an eye-lid with diplopia occurring in an otherwise healthy person is the result of cerebral syphilis in a large proportion of cases, and this is true also of sudden and rapidly progressing deafness. The Argyll-Robertson pupil is observed less frequently in meningo-vascular syphilis than in general paresis and tabes.

When the meningo-vascular disease involves the spinal cord there may be a girdle sense, pains in the limbs, bladder disturbances, etc., followed by definite evidences of myelitis, either focal or diffuse. Spinal symptoms, like the cerebral, are subject to remissions and regressions. The symptoms of syphilis of the cerebral arteries are similar to those of ordinary arteriosclerosis affecting the brain and include vertigo, sudden attacks of unconsciousness or of brief mental confusion, and transient disturbances of speech. Hemiplegia is of frequent occurrence and coming on in a person under 45, especially if unaccompanied by loss of consciousness, is very likely to be of syphilitic origin. If the perforating arteries are especially involved the symptoms may be those of pseudo-bulbar palsy.

Of the parenchymatous nervous diseases due to syphilis general paresis and tabes dorsalis are by far the most common. These affections are considered on pages 974 and 978 respectively. Primary optic atrophy is usually observed in association with tabes (20 per cent. of cases) or general paresis (4 per cent. of cases), but occasionally it occurs alone as a direct result of syphilis. The symptoms of Erb's syphilitic paraplegia appear to be those of a mild or partial transverse dorsal myelitis and comprise gradually developing paresis of the legs, increase of the deep reflexes, interference with micturition, and slight sensory disturbances. Erb regarded the condition as a distinct variety of syphilis of the spinal cord, but according to Oppenheim

and Marie it is really a clinical expression of syphilitic meningo-myelitis. Among other systemic diseases of the motor tracts that may sometimes be traced to syphilis are lateral sclerosis, amyotrophic lateral sclerosis and progressive spinal muscular atrophy.

Disease of the *peripheral nerves* without coexistent lesions of the central nervous system is an unusual result of syphilis, but is occasionally observed. Clinically nerve-syphilis may manifest itself as neuralgia, as root neuritis or as polyneuritis. Of the cranial nerves, the trigeminus is most often affected. Occasionally arsphenamin injections are followed after an interval of weeks or months by disturbances in certain of the cranial nerves, especially the auditory nerve (deafness, tinnitus, vertigo, etc.). In the majority of cases, these so-called neurorecurrences are the result of the syphilis, but in some instances they may possibly be due to the arsphenamin or to a Herxheimer reaction to the arsphenamin. A few cases of syphilitic polyneuritis are on record. Finally, it must always be remembered that syphilis may be responsible, at least in part, for certain functional disturbances, such as epilepsy, migraine, and neurasthenia.

## Congenital Syphilis

When syphilis becomes fully developed *in utero* the embryo or fetus frequently dies and abortion or premature birth take splace. The premature child when stillborn is usually shrivelled and macerated. Living children born of syphilitic parents may show unmistakable signs of the disease at birth, but this is somewhat exceptional. In the majority of cases clinical manifestations do not appear until the third or fourth week, and in some instances months or years elapse before any symptoms are present (late or tardy congenital syphilis). In another group of cases the child remains apparently healthy throughout life, although the blood gives a positive Wassermann reaction (latent congenital syphilis). Finally, children normal in every respect are sometimes born to luetic parents. In 350 pregnancies Nonne found that 26 per cent. ended in abortions and 2.9 per cent. in stillbirths. Of the living children 18.8 per cent. died soon after birth and at least 35.8 per cent. of the survivors were pathologic. Generally speaking, the later the stage of syphilis in the parents the less the severity of the disease in the child.

Among the symptoms that are sometimes present at birth the most frequent are malnutrition, a vesicular or bullous eruption (pemphigus neonatorum), coryza ("snuffles") and enlargement of the liver and spleen. Jaundice the result of intercellular cirrhosis is occasionally observed and doubtless choroido-retinitis is present in some cases. The so-called white pneumonia of Virchow may be found at autopsy even in infants who have lived for several hours. General undersize (microsomia) and lack of resistance are frequent. According to many writers some etiologic relationship exists between hereditary syphilis and certain congenital malformations, such as cleft palate, spina bifida, polydactylism, etc., but this is doubtful. It is indisputable, however, that congenital heart disease, especially interstitial myocarditis, and congenital deafness from changes in the acoustic nerve may have a luetic origin. A proportion of the cases of hydrocephalus and of spastic paralysis are also due to hereditary syphilis.

After birth congenital syphilis shows itself most frequently in marasmus, coryza, certain skin eruptions, enlargement of the liver and spleen, epiphysitis and other bony changes, interstitial keratitis, and mental deficiency,

but affections of the joints, central nervous system and viscera other than the liver and spleen are by no means uncommon.

*Marasmus.*—Progressive wasting is noticeable in a large majority of cases. It is independent of any digestive disturbance, although attacks of enteritis are common. The skin is muddy and inelastic, the expression is listless, and the general appearance of the infant is often that of a weazened old man. If the child survives, its growth is frequently stunted. In older patients anemia is sometimes pronounced and occasionally it is the chief or, at the time, the only indication of the disease.

*Snuffling.*—Coryza is present in about three-fourths of the cases. It may increase the inanition by interfering with suckling. Necrosis of the nasal bones and cartilages sometimes ensues leading to depression of the bridge of the nose (saddle-nose) or there may be an extension of the inflammation to the pharynx, Eustachian tube and middle ear with the production of otorrhea and perhaps deafness. Laryngitis indicated by a hoarse cry often accompanies the coryza.

*Skin Eruptions.*—An eruption occurs about as frequently as the snuffling, the most characteristic being a desquamative dermatitis affecting chiefly the palms of the hands and the soles of the feet or a yellowish-red or reddish-brown macular rash beginning about the perineum and tending to spread to the thighs and trunk. Bullous lesions with a predilection for the palms and soles are occasionally observed. Mucous patches may be found in the usual situations on the skin and mucous membranes. Chronic fissures or striæ (rhagades) are common about the lips, especially at the angles of the mouth.

*Visceral Lesions.*—Enlargement of the liver and spleen is present in many cases, and is significant, although by no means pathognomonic. Acute nephritis is an occasional feature. Hemoglobinuria is comparatively rare, but is of diagnostic import. In a certain proportion of the cases of cardio-vascular disease observed in early childhood congenital syphilis is the basic factor. Orchitis, usually painless, is not uncommon and is very characteristic. It frequently ends in atrophy of the organ.

*Changes in the Bones, Joints and Teeth.*—Bony changes, especially epiphysitis and gummatous periostitis, are common. Epiphysitis usually affects the long bones and may cause not only tenderness and swelling but also crepitation. In some instances the inflammatory process extends to the overlying muscles and gives rise to "syphilitic pseudo-paralysis," a condition that should be suspected when an infant during the first six months loses the use of one limb without apparent cause. Periostitis affects especially the tibia and leads to permanent thickenings and deformities. A sluggish inflammatory swelling of the phalanges (syphilitic dactylitis) occasionally develops and may proceed to abscess formation. Onychia and paronychia may also occur. Deformities of the cranium, particularly a bulging of the frontal eminences ("Olympic forehead"), is not rarely observed in children who have outlived the more active manifestations of the disease. Rachitis is not an expression of hereditary syphilis, as Parrot assumed, but the two diseases often coexist. Joint lesions are comparatively rare, but chronic synovitis and osteoarthritis are sometimes observed.

The teeth are often undersized and irregularly placed. Especially characteristic, however, although somewhat unusual, are the changes that Hutchinson described in the upper central incisors of the permanent teeth. These teeth are short and broad, are narrower below than above, and present a single crescentic notch at the free edge.

*Eye and Ear Changes.*—The most common ocular affection of congenital

syphilis is interstitial keratitis. This condition, which usually attacks both eyes in succession, is a comparatively late feature, but is almost pathognomonic, constituting with bilateral deafness and the notched teeth the diagnostic triad of Hutchinson. It is characterized by increasing opacity of the cornea (ground-glass appearance), ciliary injection, dimness of vision and photophobia. Choroiditis and iritis may also occur, but are relatively infrequent. In a large series of nurslings Scherer and Kutvirt[1] found otitis media in 22.5 per cent. of the congenitally syphilitic.

*Nervous Affections.*—Mental deficiency varying in degree from slight enfeeblement of intellect to actual idiocy, pachymeningitis with cortical sclerosis, cerebral palsies and hydrocephalus are not infrequently the result of congenital syphilis. This is true also of epilepsy. In juvenile tabes there is almost always evidence of hereditary lues. Acute meningitis is a rare expression of infantile syphilis (Ravant and Darré, Mott, Hutinel).

**Diagnosis of Syphilis.**—If the primary lesion is not wholly characteristic no time should be lost in waiting for the development of enlarged lymph-nodes and cutaneous rashes before making the diagnosis, but careful search should be made for the spirochæta pallida. This organism is most likely to be found in secretion secured from the deepest part of the lesion, and is best demonstrated by dark-field illumination. In case of doubt a positive opinion should not be given until the examination has been repeated several times. Demonstration of the spirochætæ as a means of diagnosis is applicable not only to the primary sore, but also to mucous patches and early ulcerative lesions. Even the typical soft chancre should always be investigated microscopically, as it not rarely harbors the organism of syphilis.

The diagnosis of visceral syphilis is based chiefly upon the patient's past history with regard to the initial and secondary symptoms, upon the existence of the scar of a primary sore, upon the presence of active, latent or obsolete syhpilitic lesions in the more accessible parts of the body, such as general enlargement of the lymph-nodes, periosteal thickenings, atrophic pigmented cutaneous scars, deforming cicatrices in the pharynx or nose, indurative atrophy of the base of the tongue, etc., and above all upon a positive result with the Wassermann test. In women a history of repeated abortions is suggestive. Of course a positive Wassermann reaction and other signs of syphilis are not always to be accepted as proof that the visceral disease from which the patient is suffering at the time is of a syphilitic nature; indeed, evidence of syphilis in the patient may be irrefutable and yet the clinical findings in the condition for which he seeks advice may point unequivocally to some other etiologic factor. Among the conditions in which it is especially important not to overlook the possibility of syphilis as the basic factor may be mentioned: obscure nervous diseases, both functional (epilepsy, headache and neurasthenia) and organic, enlargements of the liver and spleen, especially if the associated symptoms are of a bizarre character, atypical infiltrations in the lungs, unusual forms of renal disease, heart-block and other cardiac arhythmias, certain grave anemias, chronic joint diseases otherwise unexplained, long-continued fever without obvious cause, and paroxysmal hemoglobinuria.

The *Wassermann reaction* (see p. 175) is sometimes positive as early as the fifth or sixth day after the appearance of the chancre, but in many cases it cannot be demonstrated until the third or fourth week, and occasionally it is positive only after the sixth or seventh week. A positive reaction can be obtained at one time or another in about 90 per cent. of all cases of untreated and active tertiary syphilis and in at from 50 to 75 per cent. of long-standing

[1] Jahrb. f. Kinderh., 1915, lxxxii, 249.

latent cases. In untreated congenital syphilis the reaction is almost invariably positive. If such diseases as leprosy, frambesia, sleeping sickness, and pellagra, which have sometimes given a positive result with the Wassermann test, can be excluded, a well-marked positive reaction (complete inhibition of hemolysis or the four-plus of some writers) may be regarded as specific. A positive diagnosis should never be made, however, upon a doubtful reaction, nor should a single negative test be regarded as proof of the absence of syphilis if clinical signs are present suggestive of the disease. In doubtful cases the cerebrospinal fluid should also be tested, as it sometimes yields a positive result when examination of the blood is negative, and before a final opinion is expressed recourse should be had to the so-called provocative Wassermann reaction, which consists in administering a small dose of arsphenamin previous to examining the blood or cerebrospinal fluid in the usual way. It is said that the ingestion of alcohol within twenty-four hours of the Wassermann test is capable of rendering a positive reaction negative (Craig and Nichols).

Noguchi has found that in many syphilitic patients the intracutaneous injection of a small quantity (0.07–0.1 mil) of a devitalized and sterile emulsion of different cultures of spirochæta pallida is followed by an allergic reaction comparable to that produced by tuberculin in tuberculosis. The prepared emulsion is known as *luetin* and the reaction is considered to be positive when the injection is followed by the development of a papule or pustule with erythema at the site of inoculation. Owing to the occurrence of retarded reactions the patient should be observed for two weeks. Although specific and simple, the luetin reaction is, on the whole, less reliable than the Wassermann reaction. It may be absent when the Wassermann reaction is strongly positive or the reverse. It is chiefly useful as a check on the Wassermann reaction in tertiary, congenital and latent syphilis, particularly in cases under treatment. It is of little value in primary and secondary syphilis. It has been shown that persons taking potassium iodid may yield a positive luetin reaction whether syphilis is present or not.

The chemocytologic changes that occur in the *cerebrospinal fluid* in a large proportion of cases of syphilis have been found of definite value in demonstrating an early involvement of the nervous system by the spirochete and also in differentiating between the later cerebrospinal manifestations of the disease, such as meningo-encephalitis, tabes, paresis, etc., from conditions simulating them. The most important of these changes are an excess of globulin, pleocytosis, and Lange's "luetic curve" with colloidal gold. Normally, the cerebrospinal fluid contains but a trace of albumin, but in meningitis from any cause and in the various forms of cerebrospinal syphilis an excess of albumin in the form of globulin is commonly present. Accompanying the globulin reaction there is usually an increase in the number of lymphocytes beyond the normal limits, which may be considered to be from 5 (von Kafke) to 10 (Nonne) per cubic millimeter. In some cases the number is 100, 200 or even more. Increase in albumin and globulin and pleocytosis are not rarely observed even in the primary or preroseolar stage, when only the chancre is present, (Wechselmann, Wile and Stokes, Wile and Hasley[1]). Similar deviations from normal spinal fluid occur also in many cases of congenital syphilis (Jeans, With, Ravaut, Kingery[2]). Doubtless early infection of the nervous system may be only transitory.

Lange's colloidal gold test is based upon the observation that substances in pathologic spinal fluids, especially in spinal fluids of luetic patients, will

[1] Jour. Amer. Med. Assoc., Jan. 1, 1921.
[2] Jour. Amer. Med. Assoc., Jan. 1, 1921.

precipitate colloidal suspensions with resultant color changes, provided the globulin and nucleoprotein fractions are held in solution with a 0.4 per cent. sodium chloride solution. The color changes depend upon the amount of gold precipitated in 10 dilutions of spinal fluid in geometrical progression from 1 to 10 to 1 to 5120 and may be plotted in curves which take on certain characteristics for different conditions. Fluids from patients who have syphilis of the central nervous system give their maximal reactions in the lower dilutions, and this change is so constant that it has been spoken of as the "luetic curve." The colloidal gold test is very delicate and is sometimes positive in syphilis when the Wassermann test is negative.

**Prognosis of Syphilis.**—So far as absolute cure is concerned the prognosis is more or less uncertain. Manifestations in one form or another may reappear after latent periods of 2, 3, or even 4 decades, and evidences of infection may not rarely be found at autopsy in the heart, testis, or some other organ when for many years before death all clinical signs were absent and even the Wassermann reaction was negative. Nevertheless, it is certain that spontaneous cure sometimes occurs and that with early and adequate treatment the infection may usually be kept in complete abeyance, if not altogether extinguished. In general, there is no relation between the severity of the early manifestations and the likelihood or the gravity of remote effects, the future of the patient being determined almost entirely by the time at which treatment is instituted and the thoroughness with which it is carried out. The prognosis as to cure must be especially guarded in all cases first treated during the tertiary periods. There is yet no way of determining with exactness in a given case when recovery has actually taken place. It is only when the clinical and serologic findings have been constantly negative, on repeated examinations, for many years, that the probability of complete cure is to be assumed. At least 20 per cent. of the late and hereditary cases and from 30 to 40 per cent. of the cases of neurosyphilis and cardio-vascular syphilis, despite thorough treatment and regardless of the degree of symptomatic improvement, remain persistently Wassermann positive. The percentage of infected persons who die of the disease cannot be definitely stated but in view of the important part that syphilis plays in the etiology of affections of the circulatory organs and central nervous system it is probably much larger than is generally supposed. Death from the early manifestations is comparatively rare, but occasionally acute yellow atrophy of the liver, meningitis or nephritis supervenes during the secondary period and proves fatal. Cases of unusual virulence (malignant syphilis), with very severe symptoms throughout or with grave, often rapidly fatal, tertiary lesions early in the disease, are occasionally observed.

The prognosis of congenital syphilis is grave, at least one-third of all infants with symptoms of the disease dying within the first half year of life. As a rule, the longer the symptoms are in appearing after birth, the less likelihood is there of a fatal termination.

**Treatment of Syphilis.**—The only certain means of prevention is avoidance of the sources of infection. As the disease is acquired in the large majority of cases through illicit coitus, continence is, of course, the chief safeguard. Accidental infection, however, is not infrequent, and therefore the patient should be told of the danger of transmitting the disease by kissing, by contaminating utensils that others are likely to use, etc. The prophylactic treatment suggested by Metchnikoff which consists in rubbing a 33 per cent. calomel ointment into the penis and foreskin after infective contact has been employed in armies and navies with considerable success. The use of the ointment before coitus still further lessens the danger of infection.

Fournier and Guenot,[1] Lacapère and Laurent,[2] Michel and Goodman,[3] report favorably on the abortion of syphilis by moderate doses of arsphenamin used during the primary incubation period.

Marriage should be prohibited to a syphilitic person until at least 4 years after the date of infection and even then if thorough treatment has not extended over 3 years and all symptoms have been absent for at least one year. If marriage should occur before the time specified and the wife conceive, she should undergo active treatment throughout the whole period of pregnancy.

As to public prophylaxis, instruction of the laity about syphilis itself and the menace to health of prostitution and the establishment of free dispensaries and provision in all general hospitals for the treatment of veneral diseases are the most hopeful means of controlling the spread of the disease. State regulation of prostitution has proved ineffectual.

For the *local treatment* of the primary sore reference must be made to surgical works. The experiments of Neisser upon apes and of Brown and Pearce upon rabbits demonstrate the futility of excision. These observers found that there is no appreciable time during which the infection can be regarded as confined to the portal of entry.

*Constitutional treatment* should be begun as soon as the diagnosis is certain. The three potent internal remedies are arsphenamin and its allies, mercury and iodin, preferably in the form of potassium iodid. Of these remedies, probably only the first two have spirochæticidal action. Arsphenamin suppresses the manifestations of syphilis more rapidly than any other drug, and there is little doubt that many patients are cured by repeated doses, especially when it is used early and is alternated with mercury. The intravenous method of administration is now employed almost exclusively, and as there is considerable danger of pheblitis and of sloughing of the tissues under certain conditions, only persons who have been properly instructed in the procedure should attempt it.

The dose of arsphenamin and the frequency of its administration vary with the stage of the disease, the general health of the patient, the age, and the sex. For robust men with active syphilis the maximum dose is 10 gr. (0.6 gm.). For less vigorous men and for women the dose should be from 4 to 8 gr. (0.25 –0.5 gm.), and for children, 2 to 5 gr.(0.13–0.3 gm.). Neoarsphenamin has advantages over arsphenamin in being readily soluble in water and of neutral reaction, but, it seems to be somewhat less effective than the older preparation. The maximum dose is 15 gr. (0.9 gm.). Arsphenamin should be given with at least 120 mils of saline solution for each 10 gr. (0.6 gm.) and introduced into the vein, preferably one at the elbow, from a gravity buret. In preparing the saline solution only freshly distilled water should be used. The arsphenamin should be dissolved in about 50 mils of hot saline solution and then alkalinized with sodium hydroxid (23 drops of a 15 per cent. solution), the latter being added a drop at a time and the solution well shaken after each drop until the fluid becomes clear. Finally, enough cold saline solution should be added to bring the total amount up to 120 mils. The solution should be used at once after it is made. Not less than 5 minutes should be allowed for the 120 mils to enter the vein. The patient should be recumbent during the treatment and should remain so for several hours after it.

Solutions of neoarsphenamin may be administered from a buret by the

[1] Presse méd., 1919, xxvii, 554.
[2] Bull. med., 1919, xxxiii, 539.
[3] Jour. Amer. Med. Assoc., Dec. 25, 1920.

gravity method or directly from a Luer syringe. For intravenous injection the drug should be dissolved, with but slight agitation, in from 50 to 20 mils of freshly distilled, warm (75° F.), sterilized water. Unless the solution is brilliantly clear it should be rejected, as cloudy solutions invariably cause severe reactions. For intramuscular injections a Luer syringe should be used with needles 1½ to 2 inches long. The injections are best made into the buttocks. About 3 mils of freshly distilled water should be used for each 2½ gr. (0.15 gr.) of neoarsphenamin.

Not rarely injections of arsphenamin or neoarsphenamin, especially of the former, are followed by lumbar pains, chills, fever, nausea and vomiting. These effects usually subside within 24 or 36 hours and are not serious. In another and much smaller group of cases the symptoms occur after 2 or 3 days and consist of headache, vomiting, extreme weakness, albuminuria and oliguria or actual suppression of urine. Jaundice may also develop and coma may supervene. Death may result from collapse, uremia or hemorrhagic encephalitis. In other cases a reaction, apparently of an anaphylactic nature, occurs after the second injection or a later one and is characterized by a sense of suffocation, flushing of the face or cyanosis, and sometimes chill, fever, and an urticarial or a diffuse erythematous eruption. In some cases, probably as a result of the liberation of a large amount of luetic toxin, the syphilitic eruption is temporarily intensified by the injection (Jarisch-Herxheimer reaction).

Occasionally, arsphenamin injections are followed by neuritis. In the presence of advanced disease of the circulatory organs, kidneys, or gastrointestinal tract of other than luetic origin, or of any intercurrent acute infection the drug should be used in minimum doses or not at all.

As a rule, arsphenamin or neoarsphenamin is best given every few days or a week for 5 or 6 injections, the intervals being used for the administration of mercury. Between each course of the drug a rest period of 6 weeks is usually advised. In primary syphilis at least two courses with six months of mercurial treatment should be given, even if the Wassermann reaction is negative. In secondary syphilis it is often necessary to give 3 or 4 courses of arsphenamin with mercury before the serum reactions become negative. Some syphilographers advocate a short course of mercury before the injections of arsphenamin in florid syphilis, hoping in this way to avoid the intensification of the rash that sometimes follows arsenical treatment. In tertiary syphilis it is advisable to combine the courses of arsphenamin with the prolonged use of both mercury and potassium iodid. Indeed, in tertiary lesions of the viscera and bones, as well as in latent syphilis with a positive Wassermann reaction, better results are not rarely secured from the prolonged use of mercury and potassium iodid than of arsphenamin alone. In all cases prolonged medical supervision is necessary, for it is only when the clinical and serologic findings are constantly negative, on repeated examinations for many years, that we can regard the cure as probable. An isolated negative Wassermann reaction, especially in the absence of a provocative injection of arsphenamin, is no criterion that the infection is extinct. With persistently positive serologic findings a course of treatment should be given annually or biannually.

The intraspinal use of arsphenaminized serum, as elaborated by Swift and Ellis, is a distinct advance in the treatment of syphilis of the central nervous system, especially of gummatous infiltrations, and to a less extent of tabes and general paresis. The technique is briefly as follows: An hour after an intravenous injection of arsphenamin or neoarsphenamin, 60 mils of blood are withdrawn by venepuncture. The serum of this blood, after being diluted

with normal saline solution to form a 40 per cent. mixture, is kept at a temperature of 56° C. for one-half hour. Later in the day a lumbar puncture is made and an amount of fluid equivalent to the amount to be introduced is withdrawn. While the needle is still in place 30 or 35 mils of the diluted serum are allowed to flow into the subarachnoid space by gravity through a rubber tube (40 cm. in length) connected to the barrel of a Luer syringe. After the treatment the patient should be kept in bed with his feet slightly elevated for twenty-four hours. Untoward symptoms, such as headache, pains in the legs and vesical disturbances are sometimes noted. The treatment is repeated at intervals of from 10 days to 2 weeks and for 4 to 6 administrations according to the patient's tolerance. In some cases better results are secured by omitting the preliminary intravenous injection and using serum which has been heated and to which has been added directly the arsphenamin. The primary dose of the latter should not exceed ¼ milligram (Ogilvie's method).

Mercury may be given in syphilis by the mouth, by inunctions or by intramuscular injections. By the mouth, the favorite preparations are the protoiodid (¼ gr., 0.015 gm.), the biniodid (1/16 gr., 0.004 gm.) and for children, mercury with chalk (1 gr., 0.06 gm.). Whatever preparation is selected or whatever method of administration is employed, the dose should be the maximum the patient can tolerate, and the treatment should be given in courses of 5 or 6 weeks duration, with intermissions of from 1 to 3 months, for 2 years or longer, according to the clinical and serologic findings. During the administration of the mercury the teeth should be brushed after each meal and the mouth should be cleansed several times a day with a mild antiseptic wash.

Inunction is an effective method of administering mercury and has the advantage of not disturbing the digestion. The disadvantages of the method are the publicity that it entails, its unpleasantness, and the uncertainty of the dosage. It is carried out by rubbing 30 grains (2.0 gm.) of fresh mercurial ointment thoroughly into the skin every day for six consecutive days, a different area being selected for each inunction, so as to avoid irritation. On the seventh day a warm cleansing bath is substituted for the rubbing. Favorite sites are the inner sides of the arms and thighs, the groins, the chest and the abdomen. The treatment should be continued for 5 or 6 weeks and then omitted for from 1 to 3 months.

Intramuscular injections of mercury yield excellent results. They permit of more exact dosage and more close supervision of the patient than oral administration or inunction. On the other hand, they are more or less painful and occasionally result in serious toxic symptoms, especially if insoluble preparations are used. Soluble salts act more promptly but cause more pain. A freshly made 1 per cent. solution of mercuric benzoate in distilled water, with the addition of 2.5 per cent. of sodium chlorid, may be injected daily in doses of 30 to 45 minims (2.0–3.0 mils) with comparatively little pain. The injections should be made into the gluteal muscles every day or every other day in courses lasting from 4 to 6 weeks, and then discontinued for about six weeks. One of the best of the insoluble preparations, if carefully compounded, is gray oil, a 40 per cent. suspension of metallic mercury in oil. Of this 5 min. (0.3 mil) may be given once a week for a period of from eight to twelve weeks.

The iodids have no spirochæticidal action, nevertheless as adjuvants to arsphenamin and mercury they are invaluable, especially in tertiary and latent cases and those involving the nervous system. It has been suggested that their resorptive action on syphilitic deposits favors the access of arsenic

and mercury to the spirochætæ. Although moderate doses are sometimes sufficient, it is generally advisable to increase the amount gradually until 2 or even 3 drams (8.0–12.0 gm.) are being taken daily. Milk is the best vehicle. In some cases an iodid may be advantageously combined with mercury, as in the following formula:

℞. Hydrargyri chloridi corrosivi ..... gr. i (0.065 gm.)
Potassii iodidi ..... ʒiii–ʒi (12.0–30.0 gm.)
Syrupi sarsaparillæ compositi ..... fʒii (60.0 mils)
Aquæ ..... q. s. ad fʒiv (120.0 mils) M.
Sig.—Two teaspoonfuls in water three times a day after meals.

Iodids have no place in the treatment of the early manifestations of syphilis.

Aside from specific medication, general hygienic measures are of the utmost importance. The use of alcohol should be interdicted and the patient should be warned against excesses of all kinds. In some cases, especially if the nervous system is involved, complete rest at least for a time, is imperative. When there is cachexia much benefit accrues from the use of iron and bitter tonics.

*Syphilitic infants* until they are a year old are best treated by mercurial inunctions or the administration of mercury with chalk. The inunctions are usually made over the abdomen, mercurial ointment of one-fourth to one-half strength being employed for the purpose. After the first year arsphenamin may be given in doses of 0.01 gram for each kilogram of body weight.

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## MALARIA

(Malarial Fever; Ague)

**Definition.**—Malaria is an infectious disease due to a primitive unicellular organism belonging to the class Sporozoa, transmitted by the bites of infected mosquitoes, and characterized by a symptom complex which shows a marked tendency to pursue a paroxysmal course and to recur periodically. In typical cases definite chills occur every other day (tertian malaria), every third day (quartan malaria), or at more or less irregular intervals (estivo-autumnal malaria).

**History.**—Malaria has been known for several thousand years and Hippocrates gave an accurate description of it as early as 400 B.C. Until recent times, however, it was generally regarded as a miasmatic affection excited by noxious vapors from swamps, marshy soil, or pools of stagnant water. The modern conception of the etiology of malaria dates from 1880 when Laveran[1] discovered in the blood of malarial patients a parasite which he believed to be the specific cause of the disease. Laveran's observation was soon verified by Richard, Marchiafava and Celli, Sternberg, Councilman, Osler and others. Later in 1885, Golgi[2] described the life cycle of the parasite of quartan malaria in man and pointed out that the malarial paroxysm is always synchronous with the sporulation of a group of parasites. In 1897 MacCallum[3] showed that the flagella appearing at the circumference of certain organisms are essential elements in the process of fertilization. The

[1] Bull. de l'Acad. de Méd. de Paris, 1880.
[2] Arch. per le scienz. Med., 1886.
[3] Bull. of Johns Hopkins Hosp., Nov., 1897.

same year Ross[1] was able to demonstrate the life-cycle of the parasite in the mosquito. Later he succeeded in infecting healthy sparrows by allowing them to be bitten by mosquitoes that had previously fed on sparrows sick with a form of malaria. The following year, 1898, Bignami[2] and Grassi[3] were successful in producing malaria in man by the bites of infected *Anopheles*.[4] Many similar experiments were successfully made in different parts of the world and to-day it is a firmly established fact that mosquitoes act as intermediate hosts of the parasite and convey the infection to man by direct inoculation. In 1911 Bass[5] first cultivated the parasites of malaria.

**Etiology.**—The specific cause of malaria is an animal parasite of the protozoan group commonly known as the *Plasmodium malariæ* of Laveran. While the exact position of this organism in the biologic scale is somewhat doubtful, most authors regard it as a member of the class *Sporozoa*, and order *Hemosporidia*. It is a true parasite living at the expense of the red blood cells. Intracorpuscular forms akin to it are found in many of the lower animals, but they are of a different species and, as Koch first demonstrated, are not pathogenic for man.

There are at least three species of parasites concerned in the production of human malaria: *Plasmodium vivax*, or tertian parasite, *Plasmodium malariæ*, or quartan parasite, and *Plasmodium falciparum*, or æstivo-autumnal parasite. These three species cause all the manifestations of the disease and each produces its own clinical type. All three forms have certain morphologic and biologic features in common. They consist of a protoplasmic body and a vesicular nucleus, provided with particles of chromatin; they possess ameboid movements; they multiply by a process of fission which is equivalent to sporulation; and they have two phases of existence, an intracorpuscular or human phase which is asexual and an extracorpuscular or mosquito phase which is sexual. So far as is known the conditions necessary for the existence of these parasites are to be found only in the blood of human beings and in the bodies of certain mosquitoes.

*Plasmodium Vivax.*—If a specimen of blood from a patient with tertian malaria be examined with a one-twelfth immersion lens shortly after a chill certain of the erythrocytes will be found to contain a small, round pale body, with a vacuole in its center and its protoplasm condensed at the periphery into the form of a ring (*trophozoite*). In a drop of blood drawn six or eight hours later the organism will be observed to be considerably larger, more distinct and actively motile. Toward the close of the first twenty-four hours following the chill pigment derived from the hemoglobin of the infected corpuscle begins to appear in the interior of the parasite. The pigment consists of black or brownish granules which for a time are grouped in the form of a ring near the periphery of the protoplasm. Through the action of protoplasmic currents the individual granules are kept in constant oscillation. The parasite reaches maturity in from 36 to 40 hours. It is then nearly as large as the red corpuscle, deeply and diffusely pigmented, but without ameboid movements (*schizont*). During the evolution of the plasmodium the erythrocyte becomes swollen and progressively paler. At the

[1] Report on the Cultivation of Proteosoma (Labbé) in Gray Mosquitoes. Calcutta, 1898.
[2] Lancet, Dec. 3, 1898.
[3] Rend. R. Accad. d. Lincei, Roma, 1898.
[4] The theory that malaria was transmitted by mosquitoes was held by the Roman writers nearly two thousand years ago. It was vigorously supported by J. E. Nott, of Mobile, in 1848, and again by A. F. A. King, of Washington, in 1882. It was elaborated and clearly formulated by Patrick Manson in 1894. Ross, however, deserves the credit for having proved it experimentally.
[5] Jour. Amer. Med. Assoc., Nov. 4, 1911.

end of 48 hours sporulation takes place. The pigment collects in the center of the parasite and the nucleus and cytoplasm divide, forming a rosette-like figure composed of 15 to 20 segments or spores (*merozoites*). With the completion of sporulation the erythrocyte disintegrates, thus liberating the spores or merozoites, which at once invade other erythrocytes and go through the same asexual life cycle (*schizogony*) as the parent parasite. The liberated pigment is taken up by phagocytes and is ultimately deposited in the various organs. A period of from 8 to 12 days after the bite of the mosquito is required for the infection to become sufficiently severe to produce symptoms. This period constitutes the *incubation period*. The chills are probably due to a toxin that is set free in the blood stream at the time of sporulation.

Several weeks after infection, sexual forms of the parasite appear in the peripheral blood. The female form (*macrogametocyte*) is rich in pigment, but its nucleus is poor in chromatin, and the male form (*microgametocyte*), the smaller of the two, is poor in pigment, but its nucleus is rich in chromatin. In the stomach of the female anopheline mosquito these sexual forms undergo reduction, the macrogametocyte becoming a *macrogamete* and the microgametocyte a *microgamete*. The latter is a free-swimming thread of protoplasm analogous to a spermatozoön. The microgamete fertilizes the macrogamete, producing a *zygote* or *oökinete*. The oökinete bores into the stomach wall of the mosquito and there becomes encysted (*oöcyst*). In the course of a few days the contents of the oöcyst break up in a number of minute spherical bodies, known as *sporoblasts*. By another process of nuclear and cellular division each sporoblast is transformed into numerous slightly curved nucleated filaments (*sporozoites*). Finally the oöcyst breaks and the sporozoites enter the body-cavity of the mosquito, many of them finding their way into the salivary gland from which they are readily inoculated into the human being when the insect again bites. On entering the blood of man the sporozoites penetrate the red corpuscles and become trophozoites exactly as do the segments from the roset of the asexual cycle. Under favorable condition sexual reproduction (*sporogony*) in the mosquito is complete within about two weeks. It is likely that the sexual forms of the parasite soon perish when they are not removed from the blood of the human host by the mosquito.

*Plasmodium Malariæ*.—The parasite of quartan malaria is throughout smaller, more dense, and more sharply outlined than that of tertian malaria, but it is only after the stage of pigmentation has been reached that the one organism can be distinguished with certainty from the other. The well developed quartan trophozoite often appears as an equatorial band running across the red corpuscle, and compared with the tertian trophozoite its ameboid movements are feeble and its pigment granules are coarse, dark, and sluggish. The infected red corpuscle, too, instead of becoming large and pale as in tertian malaria, tends to shrink and grow darker. The mature quartan parasite (schizont) divides into 6 to 12 segments and these are usually more uniform in size and more symmetrically arranged than those of the tertian parasite. The whole process of asexual reproduction occupies 72 hours. The sexual life-cycle of the quartan parasite follows closely that of the tertian form. One brood of quartan parasites in the blood of man excites a chill every fourth day. If two broods coexist a chill occurs on each of two successive days, separated by one day of intermission. If three broods coexist a chill occurs every day.

*Plasmodium Falciparum*.—The youngest form of this parasite resembles that of the tertian and quartan parasites, but it is much smaller than either. As it develops, the infected corpuscle becomes dark and "brassy" in color,

shrunken and at times crenated. At an early period the parasite usually assumes the form of a small ring with the nucleus, in many instances, on the outside. Two or more rings are often seen in one erythrocyte. Compared with the tertian and quartan forms, the pigment granules are few in number and very fine. Segmentation is rarely observed in the peripheral blood, as the latter part of the asexual cycle of this organism is completed in the spleen and other internal organs. In blood aspirated from the spleen roset forms are usually numerous. The segments of the roset (merozoites) number from 8 to 10 and are irregularly placed. The time required for sporulation is variable. It may be 36 hours or more than 48 hours. Sexually differentiated forms (gametocytes) are found in the peripheral blood after a week or ten days of acute symptoms and appear in the form of a crescent, the concavity of which is often spanned by a remnant of the corpuscle. Such crescents are absolutely characteristic of estivo-autumnal malaria.

*The Mosquito.*—Malaria cannot be communicated directly from person to person except by the intravenous injection of blood containing the specific organisms. In nature the disease is transmitted from one individual to another solely by the bite of infected mosquitoes of the genus Anopheles. To become infected with malaria the Anopheles must bite a person whose blood contains the sexually differentiated forms of the specific parasite. An infective mosquito is capable of transmitting the disease for several weeks, at least, after the sporozoites have made their appearance in its salivary gland and proboscis. Anopheles mosquitoes breed chiefly in the quiet or slow running water of swamps, ditches, ponds, reservoirs and canals. During the day they rest in underbrush, shady woods, cellars and attics of houses, barns and other outbuildings, whence they issue forth in the early evening. They do not fly to any great height nor do they wander far from the place of their birth. As a rule, they do not bite by day. The female only is dangerous. Members of the genus Anopheles usually have spotted wings and when clinging to a horizontal surface hold their bodies almost at a right angle to the surface, whereas the more common Culex mosquitoes have no spots on their wings and when resting on a horizontal surface hold their bodies parallel to the surface. In both sexes of Anopheles the palpi are as long as the proboscis; in the female Culex the palpi are much shorter than the proboscis.

*Climatic and Telluric Conditions.*—Malaria is the most widely distributed of the infectious diseases. Indeed, there are few regions, except in the frigid zones, where it does not prevail to some extent. Wherever the conditions are favorable to mosquito life malaria is likely to be found. Hence, tracts of low-lying, marshy ground, situated on rivers or lakes, or in the vicinity of the sea are frequently malarial, whereas mountainous districts with well-drained soil are generally free from the disease. That the temperature of the atmosphere is an important fact is shown by the fact that the frequency and virulence of malaria steadily increase as the equator is approached. The severe estivo-autumnal infections are chiefly encountered in tropical and subtropical countries; the more benign tertian and quartan infections, while also common in warm countries, are the prevailing types in temperate regions. In the tropics the disease occurs throughout the entire year; in temperate climates the dangerous seasons are spring, summer and autumn.

In the United States the principal malarial regions are in the South, especially along the Gulf of Mexico and the Mississippi River. The benign forms are sometimes observed in the Middle States and even in the New England States, but on the whole the disease is rapidly disappearing in these

sections. In the Northern States and Canada malaria is almost unknown. In the West Indies, along the Atlantic coast line of Mexico and Central America, and along the shores of the Northern countries of South America the infection is seen in its greatest severity. Northern and Northwestern Europe are apparently free of malaria, but in the river valleys of Southeastern France and Southern Germany, along the southwest coast of Portugal and in all the countries bordering on the Mediterranean Sea it is common. Southern Asia, the Eastern Archipelago, including the Philippine Islands, and a large part of Africa are severely infected with malaria, especially the estivo-autumnal form.

*Race, Age and Sex.*—No race enjoys complete immunity, but the negro, it is affirmed, shows less disposition to the disease than the white man. Children appear to be more susceptible than adults. Sex in itself is without influence, but males being more exposed to infection, are more often attacked than females.

*Residence.*—Persons living in high-lying localities are less liable to infection than those living in low lands, because Anopheles, as a rule, does not fly very high.

*Immunity.*—One attack of malaria does not confer immunity against a second infection. However, a continuance of infection by parasites insufficient in number to produce symptoms may result in an apparent immunity.

**Morbid Anatomy.**—The changes observed in the various organs after death from malaria are primarily due to the destruction of the red blood-cells by the parasites, to the presence in the capillaries of the parasites themselves, and probably also to the action of toxins liberated by the parasites at the time of sporulation. The *spleen* is almost constantly involved. In the acute infections it is enlarged, congested, soft and more or less deeply pigmented. The follicles are indistinct. Infarts from thrombosis of the smaller vessels are sometimes present and very rarely rupture of the capsule is observed. Microscopic examination reveals great distention of the capillaries with blood-cells, many of the erythrocytes containing the malarial organisms. In the pulp are found numerous phagocytes, some of which are very large (*macrophages*) and enclose whole or partly destroyed red cells and free parasites. Pigment granules are observed in the vessel walls, in the blood corpuscles, in the pulp cells and in the trabeculæ. The pigment is composed mainly of melanin, an iron-free compound produced directly from hemoglobin through the action of the parasites, although in part it consists of hemosiderin, an iron-containing compound produced by the disintegration of the red cells, and therefore not characteristic of malaria.

In chronic malarial infections the spleen is often enormously enlarged, dark colored, and dense from an increase in its fibrous tissue (*"ague cake"*).

The liver is usually more or less enlarged and pigmented. Microscopically, the capillaries are found distended with infected red cells, phagocytes, and free pigment. The liver cells are cloudy, fatty and pigmented. Small areas of necrosis of thrombotic or toxic origin are frequently seen. In some cases the *kidneys* show the lesions of acute nephritis with pigmentation of the endothelial cells and of the tubular and capsular epithelium. Parasites may be seen both in the capillaries of the stroma and in those of the glomeruli. Changes in the *stomach* and *intestines* are seldom pronounced. In severe cases, however, the mucous membrane may show more or less pigmentation and hyperemia.

In pernicious malaria the *brain* is usually congested and of grayish-brown color. Minute hemorrhages are frequently seen in the substance of

the organ. These may be due to plugging of the capillaries with masses of infected corpuscles or of free parasites or possibly to the solvent action on the capillary endothelium of the toxin given off by the parasites. As a rule the *heart* and *lungs* present nothing peculiar.

**Symptoms.**—The incubation period of malaria usually ranges between 8 and 12 days, although it may be much longer. The symptoms vary with the type of the parasite present in the blood, the number of distinct groups or generations of parasites, and the virulence of the infection.

Tertian Malarial Fever.—This is the most common and usually the mildest of the malarial infections. It is the prevailing type in temperate climates. When caused by a single group of organisms it is characterized by the occurrence of febrile paroxysms every other day with intervals of comparatively good health. The paroxysms may appear suddenly or may be preceded by a day or two by such prodromes as lassitude, anorexia, dull headache and muscular soreness. A typical paroxysm consists of a cold, a hot, and a sweating stage.

In the *cold stage* there is a feeling of chilliness speedily developing into a severe rigor, with chattering of the teeth and shaking of the whole body. The skin is dusky and cold and presents the condition known as "*goose-flesh*," the features are pinched, and the lips are blue. Notwithstanding the coldness of the surface the temperature rises rapidly, often reaching 104° or 105°F. in the axilla toward the end of the chill. While the shivering persists the pulse is small and frequent, the respirations are hurried, and the urine is abundant and pale. Headache is generally present and not rarely there is vomiting. The cold stage usually lasts from a quarter of an hour to one or two hours.

*The Hot Stage.*—The sensation of coldness gradually gives way to a feeling of warmth and this in turn to one of intense heat. The entire surface becomes florid and pungently hot, the pulse, while remaining frequent, increases in volume, and herpes often appears about the lips. During this stage the temperature continues high and may even rise to a higher level (106°F.)than was reached during the chill. The patient is restless and complains of headache, muscular pains, and thirst. Occasionally, there is slight delirium. The urine is concentrated and frequently contains a small quantity of albumin. The hot stage usually lasts from three to five hours.

*The Sweating Stage.*—With the fall of the temperature, profuse perspiration appears, the pains subside, the thirst abates, the pulse and respiration return to their normal state, and within an hour or two the attack is over. Toward the close of this stage the patient often falls into a refreshing sleep from which he awakens somewhat languid, but on the whole feeling quite well.

The paroxysms are not always separated by an interval of exactly forty-eight hours duration. The intervals may become somewhat shorter (anticipation) when the disease is increasing in severity and somewhat longer (retardation) when it is becoming more mild.

Apart from the paroxysms the symptoms of tertian malaria are chiefly related to the spleen and blood. The *spleen* is nearly always enlarged, sometimes to such an extent that its edge can be felt projecting an inch or more below the costal margin. After one or two attacks the organ usually returns to its normal size, but after repeated infections it often remains permanently enlarged. Occasionally, there is more or less pain, or at least tenderness on pressure, over the spleen during the periods of pyrexia. The *blood* not only contains the specific organisms of malaria but it presents other

changes of great importance in the recognition of the disease. A diminution in the number of erythrocytes and a loss of hemoglobin, proportionate to the severity of the attack, follow each paroxysm. These reductions are more marked after the early paroxysms than after those occurring late (Thayer). The number of white cells is almost invariably decreased, except at the beginning of a chill, when they may be slightly increased. In 70 cases studied by Vanderhoof[1] the mean count was 4,500. A differential count usually reveals a relative increase in the number of large mononuclear forms, the proportion of these cells often rising from the normal 4 to 8 per cent. to between 15 and 30 per cent. Even when the malarial organisms cannot be found in the peripheral blood, it will usually be observed that many of the white cells, especially of the mononuclear and polymorphonuclear forms, contain granules of dark pigment. Next to the presence of the parasites

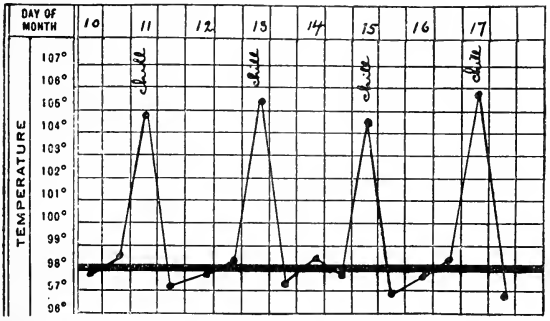


FIG. 4.—Temperature curve of benign tertian malarial infection.

themselves the occurrence of these pigmented leucocytes offers the most convincing proof that the disease at hand is malaria.

*Variations.*—Mild attacks are frequently met with, especially in temperate regions, in which the paroxysms amount to scarcely more than a moderate rise of temperature, with dull headache and general malaise, lasting three or four hours. When two broods of tertian parasites are present in the blood and each matures on successive days the paroxysms occur daily instead of every forty-eight hours (*quotidian fever*). When a number of broods are present and segmentation goes on almost continuously, fever of a *remittent type* results and the paroxysms are indicated by exacerbations of temperature. In young children the paroxysms usually lack both chill and sweating. A pinched expression with coldness of the extremities may be the only manifestation of the first stage of an attack. Vomiting and diarrhea, however, are not uncommon, and occasionally the chill is represented by a convulsion.

QUARTAN MALARIAL FEVER.—Of the three varieties of malaria, this is the least widely distributed. In certain regions, however, as in Sicily, it is the most common form. In this country it is decidedly infrequent; thus out of 616 cases of malaria studied in Baltimore, it was observed only five times (Thayer and Hewetson). With a single group of quartan parasites in the blood, febrile paroxysms occur every 72 hours (*quartan fever*); otherwise the

[1] Jour. Amer. Med. Assoc., April 20, 1907.

symptoms do not differ materially from those of tertian malaria, although generally they are somewhat more severe. When two groups of quartan parasites coexist a chill occurs on each of two successive days, separated by one day of intermission (*double quartan fever*). When three groups coexist, a chill occurs every day (*quotidian fever*). Quartan malarial fever while usually benign occasionally produces symptoms of a pernicious type.

Estivo-autumnal or Subtertian Malarial Fever.—This type prevails extensively in hot countries. In temperate regions it is much less common than tertian malaria, although it is frequently seen in the late summer and autumn. It is the most severe of the malarial infections, generally speaking, and in the tropics shows a marked tendency to excite pernicious symptoms. Estivo-autumnal fever is often referred to as remittent fever, because as it advances the paroxysms very commonly overlap one another and so prevent any actual intermissions in the febrile temperature. It should be borne in mind, however, that the disease not rarely produces an intermittent type of fever, and, on the other hand, that tertian and quartan malarial fevers are occasionally remittent.

In many cases of estivo-autumnal fever *paroxysms occur every forty-eight* hours, but as a rule, they are more severe and prolonged than those of ordinary tertian malaria. The chill may be slight or even absent, and not rarely there is little or no sweating, but the headache and muscular pains are often intense, while vomiting, diarrhea and colic are common symptoms. The rise and fall of the temperature are usually much more gradual than in simple tertian malaria, the whole paroxysm often lasting twenty-four hours or longer. Somewhat frequently the attacks begin toward evening and continue through the night and the following day. Owing to anticipation or retardation of the paroxysms, which is very common in this form of malaria, or to the presence in the blood of several generations of parasites the *fever is very prone to become remittent, continuous or irregular.* Muttering delirium and somnolence not rarely develop, and consequently without an examination of the blood, the condition may readily be mistaken for typhoid fever. In a certain group of cases there is jaundice with vomiting of bile-stained liquid and even hematemesis; hence the term *bilious remittent fever.* Less frequently estivo-autumnal fever induces *daily paroxysms* and in this event the temperature curve closely resembles that of double tertian malaria. As a rule, however, the attacks soon run into one another and a remittent type of fever results.

Estivo-autumnal fever is more resistant to treatment than other varieties of malaria, and even in temperate regions where usually only the milder forms are encountered, it often persists despite the free exhibition of quinin for two weeks or longer.

Pernicious Malarial Fever.—Frequently in tropical and subtropical countries, rarely in temperate regions, the symptoms of malaria assume a malignant or pernicious character. In the vast majority of cases the estivo-autumnal parasite is responsible for this phase of the disease, although any one of the malarial organisms is capable of exciting it. The pernicious symptoms sometimes develop abruptly during apparent good health, but more commonly they appear only after the patient has already suffered from repeated attacks of ordinary ague. According to the character of the symptoms present, four types of pernicious malarial fever have been recognized, namely, the comatose, the algid, the choleraic, and the hemorrhagic.

*Comatose Type.*—The coma may occur suddenly as the initial symptom of the disease, but far more frequently it develops gradually in the course of a febrile paroxysm, the patient becoming first delirious, then somnolent and

finally comatose. In children the coma may be preceded by convulsions. The temperature is usually high, though it may be subnormal, the breathing is often irregular and stertorous, and the pulse, while strong at first, very soon becomes feeble. The face may be extremely pale or cyanotic. In many cases there is slight jaundice. Death often occurs within twenty-four or thirty-six hours. Even when the patient rallies he is likely to suffer a relapse and to perish in the second or third paroxysm. The approach of a fatal termination is heralded by symptoms of collapse. Variations of the comatose type are not uncommon. They may take the form of aphasia, hemiplegia, epileptiform or tetanic convulsions, or symptoms of bulbar paralysis.

*Choleraic Type.*—The symptoms of this form of pernicious malarial fever closely resemble those of Asiatic cholera. There is almost constant purging, with vomiting, and moderate fever. The evacuations are copious and watery. Collapse supervenes, but not so suddenly as in the algid type of the disease. The outlook is very grave, although recovery sometimes occurs. In fatal cases thrombi composed of parasites and pigment have been found in the capillaries of the gastro-intestinal mucous membrane with secondary necrosis of the epithelial lining.

*Algid Type.*—This form is characterized by profound collapse. The entire surface of the body is cold, more or less cyanotic, and bathed with clammy sweat, the eyes are sunken, the features are pinched, the breathing is labored, and the pulse is frequent and thready. The temperature is often moderately elevated, especially at first; later it is usually subnormal. The mind is for a time clear, although inactive. Recovery is exceptional, and the duration of the a tack is not often more than 6 or 8 hours. In some instances the collapse is preceded by symptoms of colitis (dysenteric type) or fever with profuse perspiration (diaphoretic type).

Hemorrhagic Malarial Fever (Blackwater Fever, Hemoglobinuric Fever).—In certain regions, chiefly those in which the more severe forms of ague prevail, as tropical Africa, Sicily, Greece, the southern United States and Central America, malarial fever is frequently characterized by the occurrence of excessive hemolysis and the appearance of hemoglobin in the urine. This type of the disease is rarely seen in temperate latitudes, except in persons who have recently returned from infected districts. In the vast majority of cases the victim is one who has suffered from repeated attacks of malaria. While the exact cause of the condition is still somewhat doubtful, it is generally conceded that the extensive hemolysis of the red cells, with its consequent hemoglobinuria, is chiefly, if not wholly, an effect of the malarial parasite. Certain facts, however, support the view that other causes may also be operative. Thus, blackwater fever not rarely occurs when there are only a few parasites in the blood, and, on the other hand, numerous parasites may be present without the appearance of hemoglobinuria. The view first suggested by Veretas in 1858 that blackwater fever is the result of cinchonism has had many distinguished adherents (Laveran, Calmette, Tomaselli, Koch and Plehn). Without doubt the occurrence of blood in the urine after the administration of quinin in some instances has been merely a coincidence; nevertheless, the numerous cases on record in which the hemoglobinuria could be produced at will by the use of the drug make it appear reasonably certain that quinin, in some individuals, at least, may favor hemolysis and thus act as an auxiliary cause of blackwater fever. That quinin is not always the determining factor is equally attested by the numerous cases in which the hemoglobinuria developed even though not a single dose of the drug had been given. It is probable that in some instances the

destruction of the erythrocytes is aided also by cold or excessive fatigue, as in certain cases of simple paroxysmal hemoglobinuria. In other cases individual peculiarity or idiosyncrasy appears to be a factor, inasmuch as this form of malaria sometimes recurs again and again in the same person.

*Severe attacks* usually begin with chill and fever (102°–105°). An hour or two later the patient voids the dark-colored urine to which the disease owes its name. The skin is usually more or less jaundiced. Vomiting is persistent, the matters ejected consisting of bile-stained liquid. The liver and spleen, as a rule, are enlarged and tender. The patient becomes restless and depressed, then delirious, and somnolent, and ultimately in fatal cases, sinks into a comatose state. Microscopic examination of the urine shows granular masses of hemoglobin and numerous tube casts, and chemical examination, a large amount of albumin. Parasites may usually be found in the blood before an attack and at the onset of an attack, but only in about 20 per cent. of the cases after the symptoms have attained their maximum. With rare exceptions the infection is of the estivo-autumnal type. Following the paroxysm there is a pronounced reduction of both red cells and hemoglobin. In favorable cases improvement is observed on the second day. The stomach loses its irritability, the skin becomes moist, the temperature falls, the nervous symptoms subside, and the urine rapidly acquires its normal appearance. Even under these circumstances recovery is not absolutely assured, since relapse is not infrequent.

In *mild attacks* there is little or no vomiting, the jaundice is slight, nervous symptoms do not develop and the urine clears in a few hours.

Malarial Cachexia.—Persons who have had repeated attacks of malarial fever and residents of malarious districts, even if they have never had any definite febrile paroxysms, not rarely develop a condition of ill-health, known as malarial cachexia. In this condition there is marked anemia with its usual symptoms. The complexion is sallow or muddy. The spleen is enlarged and can often be felt as a smooth firm mass extending several inches below the ribs. The digestion is more or less impaired. Slight febrile attacks are common, although for long periods the temperature may be normal. In severe cases hemorrhages may occur from the mucous membranes, especially from the stomach, or into the skin or retina.

Examination of the blood shows pronounced secondary anemia, with hypoleucocytosis and a relative or an actual increase in the number of large mononuclear cells. The number of red cells may be reduced to 2,000,000 or less per cubic millimeter. Parasites are usually present, although rarely in large numbers. The condition is frequently confused with hookworm infection. Occasionally post-malarial anemia closely resembles both in symptoms and physical signs primary pernicious anemia.

Latent Malarial Infection.—This is a condition in which malarial parasites are present in the blood but do not cause any conspicuous symptoms. It is common in persons who have lived for a time in malarious localities. In such cases excessive fatigue, physical injury or exposure to cold or wet may induce fresh activity in the dormant parasites and thus precipitate a febrile attack of an intermittent or continued character. Intercurrent disease may also be the means of transforming a latent into an active infection, and in this event the malarial symptoms are likely to be overshadowed or masked by those of the superimposed ailment. A person who has latent malaria is an important source of infection to others.

**Complications and Sequels.**—The *cachexia* already described is the most common sequel. *Acute nephritis* is not rare in estivo-autumnal infections. In certain tropical regions *symptoms of colitis* are observed in large propor-

tion of cases (Craig, Jackson). *Rupture of the spleen*, usually after some slight injury, has been reported several times. A few observers mention the occurrence of *splenic abscess*. *Gangrene of the skin* has been noted by a number of authors. *Paralysis* from the accumulation of parasites in the capillaries of the brain or from peripheral neuritis occasionally supervenes. Marchiafava and Bastianelli and Bignami report cases of malaria with *bulbar symptoms*, and Torti and Spiller describe cases in which there were *symptoms of multiple sclerosis*. *Neuralgia* is not an uncommon sequel, but all cases of neuralgia which are periodic and relieved by quinin are not necessarily of malarial origin. *Melancholia*, *mania* and other psychoses have been seen, although rarely, after attacks of pernicious malaria.

Any disease may be associated with malaria. *Pneumonia* and *dysentery*, both bacillary and amebic, are somewhat frequent concomitants. Occasionally, *typhoid fever* occurs coincidentally with malaria. Such a combination of the two diseases may properly be designated typho-malarial fever, but the term is not justified unless a double infection can actually be demonstrated. The so-called typho-malarial fevers of the southern United States have been shown to be, with rare exceptions, either pure typhoid or pure malarial infections.

**Diagnosis.**—In many cases of malarial fever the diagnosis is suggested at once by the history of exposure to infection, the periodic return of fever, sweat, and chill, and the enlargement of the spleen. In a large group of estivo-autumnal infections, however, the diagnosis can only be made definitely by an examination of the blood. As the parasites, especially the young forms, are readily overlooked in fresh blood, malarial infection should not be excluded in doubtful cases until stained specimens have been carefully examined. The best time to study the blood is a few hours before a chill. In mild attacks and after the use of quinin the plasmodia may be very scarce and found only after the most diligent search. Even in the absence of parasites the presence of pigmented leucocytes is strongly suggestive of malaria and this is true also of a leucopenia with a high percentage of large mononuclear cells. The diseases with which malarial fever has most frequently been confused are typhoid fever, tuberculosis, hepatic intermittent fever, Hodgkin's disease with recurrent fever, and certain septic conditions, especially malignant endocarditis, abscess of the liver, pylelitis and osteomyelitis.

*Typhoid Fever.*—The gradual onset, the step-like ascent of the fever, and the characteristic rash usually decide the question at once, but in atypical cases with chills or a distinctly remittent fever an examination of the blood for the Widal reaction on the one hand and for the plasmodium of malaria on the other may be the only means of arriving at a correct diagnosis.

*Tuberculosis.*—When this disease presents chills, fever, and sweats but no local manifestations there is some danger of mistaking it for malaria. In doubtful cases the differential diagnosis must depend entirely upon the examination of the blood for malarial parasites, the examination of the sputum, urine, or cerebrospinal fluid for tubercle bacilli, and the results of the therapeutic test by quinin.

*Hepatic Intermittent Fever.*—The lodgment of gall-stones in the common duct is not infrequently attended by febrile attacks similar to those of malarial fever. In contrast with the latter, however, there is usually colic or at least some pain over the region of the liver; jaundice is usually present; leucocytosis is often found just before the chills, even when the count in the intervals is normal; the blood does not show plasmodia; and the quinin test is negative.

*Hodgkin's Disease.*—There is a distinct likelihood of this disease passing for

malaria when the deep-seated lymph-nodes alone are involved and recurrent pyrexia is a prominent symptom. In doubtful cases the blood examination and the therapeutic test must be relied upon in excluding malaria.

*Septic Conditions.*—In the septic processes mentioned above symptoms of local disease are rarely wanting and a decided increase in the number of polymorphonuclear leucocytes can usually be found, especially if the blood is examined soon after a febrile paroxysm. In malaria there is usually hypoleucocytosis with a relative or an actual increase of the mononuclear cells, but in uncomplicated cases virtually never a polymorphonuclear leucocytosis.

Other conditions producing malaria-like paroxysms of fever, which must sometimes be considered in the diagnosis, are *kala-azar*, *Malta fever*, and *relapsing fever*. Ague symptoms occasionally occur also in *syphilis*, in *malignant disease* and are a somewhat characteristic feature in *occupational brass poisoning* (brass-founder's ague). The resemblance of bilious remittent fever to *yellow fever* may be very close. The differentiation is considered on p. 283.

If careful attention be paid to the antecedent history, the general symptoms and physical signs, and the result of repeated examinations of the blood malarial cachexia is not likely to be mistaken for other conditions accompanied by pronounced anemia and enlargement of the spleen, such as *leukemia, pernicious anemia, secondary anemias due to intestinal parasites, hemolytic ictero-anemia, amyloidosis*, etc.

**Prognosis.**—Cases of simple tertian or quartan malaria almost invariably end in recovery if recognized early and treated sufficiently. The same may be said also of the milder estivo-autumnal (subtertian) infections prevailing in temperate regions. Relapses, however, are frequent, especially in persons who have had the disease for long periods, and are prone to occur upon change of climate or when the body resistance is lowered from any cause. In tropical countries the prognosis of estivo-autumnal infections should be guarded, although recovery is the rule when treatment is promptly and vigorously instituted. Pernicious malaria is an exceedingly grave condition and frequently ends fatally despite all treatment. The mortality of blackwater fever is from 15 to 30 per cent. Many patients with malarial cachexia recover completely under appropriate treatment, especially when they move out of the malarious district; nevertheless, the prognosis must be guarded if the symptoms are severe and of long duration.

**Prophylaxis.**—Prophylactic measures include the extermination of mosquitoes, the prevention of infection of mosquitoes, and the prevention of infection by mosquitoes (Manson). The most useful methods of suppressing mosquitoes are the efficient drainage of pools and swamps, the cultivation of damp soils and the removal of weeds and shrubs. Ponds and streams that cannot be drained or filled in should be treated every three weeks with coal-oil or, if this is not feasible, well-stocked with fish—sunfish, gold fish, top-minnows. Indispensable water tanks and cisterns should be carefully screened. For the destruction of adult mosquitoes in dwellings pyrethrum powder has been found the most satisfactory agent. The room should be sealed and a pound of the drug burned for every 1,000 cubic feet of air space. To prevent the infection of mosquitoes, malarial patients should be isolated in screened rooms. The chief means of preventing infection by mosquitoes are avoidance of sleeping in the open air, adequate protection from the insects by means of screens and self-closing devices for doors, and the use of quinin in daily doses of from 5 grains (0.3 gm.) or in a single dose of 10 or 15 grains (0.6–1.0 gm.) once a week.

**Treatment.**—Quinin is the only reliable remedy for malaria. Methylene-blue (3–5 gr.—0.2–0.3 gm.—with half its weight of powdered nutmeg) is of

some value, but it is decidedly less effective than quinin and should be employed only when there is some serious idiosyncrasy to the latter. As the youngest forms of the malarial parasites are more readily killed by quinin than the full-grown organisms within the red cells, it is usually advisable in tertian and infections to give a single large dose of the drug (15 gr. –1.0 gm.) toward the close of a paroxysm, that is when the temperature is beginning to fall. However, if the patient is seen some time after a chill, and another is not expected for thirty-six hours or more, it is better to begin the treatment at once and to give a smaller dose of quinin (10 gr.–0.65 gm.) three times a day. The remedy should be continued in such amounts until the paroxysms cease and then given in the dose of 10 gr. (0.65 gm.) once a day for at least two months. The administration of calomel as a preliminary measure increases the efficacy of quinin, probably by facilitating its absorption. Under ordinary circumstances quinin should be given by the mouth. It may be prescribed in soft capsules, in cachets or in solution. The sulphate is probably as effective as any other preparation, although it is less soluble than the bisulphate and the dihydrochlorid. To children the drug may be given suspended in syrup of yerba santa or syrup of chocolate. During convalescence arsenic and iron may be given advantageously with quinin.

In estivo-autumnal infections larger doses of quinin are usually required than in tertian or quartan malaria, although it is rarely necessary to give more than 15 gr. (1.0 gm.) three times a day. In pernicious malaria quinin should be administered intramuscularly (1 gram of the dihydrochlorid or of quinin-urea hydrochlorid in 10 mils of water, in the gluteal region, repeated once or twice) or, preferably, intravenously, 0.65 gram of the dihydrochlorid in 200 mils of salt solution, being cautiously introduced according to the arsphenamin technique.

As to the advisability of using quinin in blackwater fever there is much diversity of opinion, but the weight of authority seems to be in favor of withholding the drug during a paroxysm of hemoglobinuria unless there are numerous parasites in the blood. The intravenous method of administration, dissolving the quinin in large quantities of salt solution (300 mils), is preferred.

*General Measures.*—In acute malaria rest in bed and an easily digestible diet are requisites of treatment. During the cold stage of a paroxysm the patient should be well covered with blankets and given hot drinks. Morphin, $\frac{1}{6}$ gr. (0.01 gm.) hypodermically, is often useful in mitigating the discomfort.

In the hot stage of a paroxysm much relief is afforded by sponging the body with cool water, giving cool drinks, and administering a moderate dose of acetphenetidin or acetanilid. Persistent vomiting is best controlled by the application of a sinapism to the epigastrium and the use of such sedatives as bismuth subcarbonate, cerium oxalate, iced champagne, etc.

In the treatment of persons with latent malaria (malarial carriers) Bass[1] recommends 10 grains (0.65 gm.) of quinin sulphate every night for a period of eight weeks, or, in the event of a relapse, for longer periods. In malarial cachexia arsenic and iron are useful adjuvants to quinin. However, in many cases no decided improvement can be affected until a change of climate is secured. Splenectomy has been performed in a number of cases with gratifying results, although the mortality in this condition is relatively high (Jonnesco, Mourdas, Finkelstein, Mayo).

[1] Jour. Amer. Med. Assoc., April 26, 1919.

## INTESTINAL AMEBIASIS

(Amebic Dysentery)

Of the various parasitic forms of amebæ, two important species may be found in the intestine of man: *Entamœba coli* and *Entamœba histolytica*. The former is apparently harmless, the latter is the cause of amebic dysentery. The differences between the two species in their so-called vegetative state are not always well marked, but usually E. histolytica may be recognized by its larger size (20–60 microns), active movements, multiple vacuoles, and the sharp contrast between its coarsely granular endoplasm and highly refractive ectoplasm. In the cystic stage the differentiation is relatively easy. Cysts of E. histolytica contain four nuclei and are smaller than those of E. coli, which contain eight nuclei. Viereck's E. tetragena appears to be identical with the cystic stage of E. histolytica. The pathogenic amebæ have probably never been cultivated on artificial media. Recent studies indicate that the transmission of dysentery is due to the ingestion of the resistant encysted amebæ derived from healthy convalescents or "carriers" who give no history of dysentery, and that the motile forms found in the acute stages of the disease are relatively harmless and usually die within a few hours outside the body.

Matthews and Smith[1] found 1.5 per cent. of 450 civilians and 5.6 per cent. of 1098 healthy young recruits to be carriers of E. histolytica. The cysts can survive for weeks in moist feces and in water, but are believed to be destroyed by drying. When swallowed the nuclei develop into young amebæ, which burrow into the coats of the bowel, and there produce the infection with its characteristic lesions. The amebæ multiply by fission in the bowel until the infection tends to become quiescent, when cysts are again formed. The disease is doubtless contracted in much the same way as typhoid fever and cholera are, the encysted amebæ being introduced into the digestive tract through uncooked vegetables or fruits contaminated by the fingers of carriers or through drinking water contaminated by dysenteric stools. It is possible that flies may sometimes be a factor in transmitting the disease.

**Etiology.**—Amebic dysentery is endemic in the tropics where it is as common as the bacillary form. It is not confined to the tropics, however, but often occurs sporadically in subtropical and temperate regions. It prevails especially among the poor, and unhygienic surroundings favor its spread. Males are much more frequently affected than females and the great majority of the subjects are adults, dysentery in early life being mostly of the bacillary type. The colored race is somewhat less susceptible than the white.

**Morbid Anatomy.**—The lesions may involve the entire large bowel and even the appendix and lower portion of the ileum, but they are most common and usually most marked in the cecum and ascending colon. Infiltrations of the submucosa, due to multiplication of the fixed cells and to edema, make their appearance at various points, and later these local infiltrations undergo necrosis and are cast off as sloughs leaving ovoid or irregular ulcers, with thickened undermined edges. The floor of the ulcer may be formed by the submucosa, the muscularis, or the serosa. In advanced cases the intestine is often riddled with ulcers and greatly thickened by the formation of granulation tissue. In some instances, too, it is more or less distorted and partially occluded, as a result of cicatrization of some of the ulcers or the formation

[1] Ann. of Trop. Med. and Parasit., Feb. 28, 1919.

of adhesions between the bowel and adjacent structures. Perforations sometimes occur, resulting in localized abscesses or more rarely in diffuse peritonitis. When secondary bacterial infections supervene the process may be modified by the occurrence of diffuse catarrh, false membrane formation or gangrene.

Microscopic examination reveals the usual changes of inflammation and ulceration, with, however, very little polynuclear leucocytic infiltration, the destructive process being one of necrosis rather than of suppuration, except in those cases in which pronounced secondary infection with pyogenic organisms has taken place. Amebæ are found in the tissues at the base and edges of the ulcers, in the lymph spaces and occasionally in the portal capillaries.

**Symptoms.**—Mild forms of the disease are not rarely observed, in which for months or even years the chief symptoms are indigestion, vague abdominal pains, slight anemia, lassitude, constipation and, perhaps, some tenderness on deep palpation over the colon. The constipation may be continuous (masked amebiasis), but more frequently it is interrupted by occasional attacks of diarrhea lasting two or three days. Spontaneous recovery may ensue, or the condition may become acute, or it may gradually pass into the ordinary chronic form. In other cases the onset is sudden and the symptoms are those of acute dysentery from other causes, namely, frequent mucous and bloody discharges, more or less constant tenesmus, colicky pains, abdominal tenderness, fever (100° 102° F.), and marked prostration. In severe cases portions of sloughing mucous membrane may be passed in the stools. Death may result from exhaustion or the perforation of an ulcer, or the severe symptoms may subside and the case continue as a chronic one.

Irrespective of the mode of onset, intestinal amebiasis, like all other protozoal diseases, shows a marked tendency to chronicity. The chronic form is characterized by continuous or intermittent diarrhea, with more or less abdominal pain and tenderness. Chilling of the body, overexertion, errors of diet, and indulgence in alcohol often cause exacerbations, in which the symptoms are similar to those of the acute form, although usually less severe. Apart from the presence of the amebæ, the stools are not characteristic. In many cases, however, they are very offensive and contain considerable quantities of mucous and blood. Tenesmus is usually absent, except during acute exacerbations. The patient's general health often remains fairly good for a long period, but eventually anemia and emaciation occur, and sometimes become extreme. Edema of the feet and hands is occasionally seen. Even in uncomplicated cases there is usually a slight leucocytosis, in which the mononuclear cells are increased. Evidences of renal irritation are not uncommon.

**Diagnosis.**—Although the presence of amebiasis may often be inferred from the clinical manifestations, an absolute diagnosis can only be made by the finding of actively motile amebæ or characteristic cysts in the stools. Even when the stools are mucous and bloody and tenesmus is marked, other forms of so-called dysentery, such as may be caused by Shiga's or Flexner's bacillus (bacillary dysentery), by the *Schistosomum Mansoni* (*Bilharzia*) and by the Balantidium coli, must be excluded, as must also carcinoma, syphilis and tuberculosis of the rectum, and chronic metallic poisoning (mercury, arsenic). In bacilliary dysentery an acute course is the rule, tenesmus is usually present and is often severe, and abscess of the liver is extremely rare. The conditions necessary for a definite diagnosis are, however, the positive agglutination reactions of the dysentery bacillus with the blood serum of the patient and the isolation of the bacillus from the stools.

Among other conditions that sometimes imitate intestinal amebias may be mentioned pellagra without skin eruption and sprue.

The amebæ are usually found without difficulty, although in some cases it is necessary to make repeated examinations. The stool should always be fresh and free from urine, and if the atmospheric temperature is below 75° F., both the glass slide and the stage of the microscope should be kept warm. Not rarely amebæ are found only in stools produced by the administration of a saline purge or in flecks of mucus or shreds of necrotic tissue extracted by passing a long rectal tube.

**Complications.**—The chief complication is abscess of the liver, which is found in at least 20 per cent. of all cases examined postmortem. Males are affected much more frequently than females and the complication is rare in children. The pleural cavity or the lung is not infrequently involved secondarily by perforation of the abscess through the diaphragm, by direct extension, or by way of the hepatic veins and pulmonary artery (see p. 521). Abscess of the brain, usually metastatic from the one in the liver, is an occasional sequel. Diffuse peritonitis due to perforation of an intestinal ulcer or to rupture of an hepatic abscess, sometimes occurs, and is almost invariably fatal. Among the rarer complications may be mentioned acute appendicitis, polyarthritis, and severe intestinal hemorrhage, the last usually being secondary to abscess of the liver. Stricture of the bowel is a comparatively rare sequel. Other parasites are often found in association with the amebæ, and doubtless in some instances have a part in the production of symptoms. Thus, Trichomonas hominis, Cercomonas hominis, Lamblia intestinalis, Balantidium coli, Strongyloides intestinalis, Ankylostoma duodenale, and tapeworm may be present either singly or in various combinations. Finally, cases of mixed amebic and bacillary dysentery are not uncommon in certain localities.

**Prognosis.**—Unless the disease is far advanced it usually yields to appropriate treatment, but relapses are very common. Generally speaking, the shorter the duration of the infection, the younger the patient, and the better the general nutrition, the more favorable is the outlook. In untreated subjects the death-rate is high, although the disease often lasts for years. In some instances after the infection has been overcome and the ulcers have healed symptoms of chronic atrophic enteritis persist. Occasionally fulminating cases are observed which go on to a rapidly fatal termination despite the most approved treatment.

**Treatment.**—The general prophylactic measures recommended in typhoid fever and cholera are applicable also in intestinal amebiasis. Important factors are the selection of a pure water supply, rapid and complete disposal of fecal matter, protection of food from flies, treatment of carriers, and precautions against the handling of food by carriers. The treatment of acute cases and of all exacerbations is in general that of acute colitis from other causes, the important measures being absolute rest in bed; a diet of milk and lime-water, whites of eggs, beef-juice, milk toast, and custard; mild counter-irritation by means of mustard plasters or turpentine stupes; and the administration of a saline purge, castor oil or calomel to clear the bowels, and of some sedative, such as opium by the mouth or morphin hypodermically. Bismuth subcarbonate in large doses is also useful. When the rectum is very irritable ice suppositories or injections of warm mucilage of starch (1 ounce—30.0 mils) or of cocain solution (10 min.—0.6 mil—of a 4 per cent. solution) may be employed with advantage.

After the subsidence of acute symptoms and in all other cases the restrictions on exercise and eating need not be so severe; however, quiet living,

with many hours allotted to rest, and a diet of bland easily digestible food are imperative. Ipecacuanha in large doses has long been used as a special remedy, but it is only since 1912, when Rogers[1] employed the alkaloid emetin subcutaneously, that the value of the drug has been definitely established. It is now generally believed that emetin is a true specific, destroying the amebæ in the tissues, and that its action is comparable to the specific tropism of quinin in malaria and of arsphenamin in syphilis. It may even prevent the formation of an abscess if given early in amebic hepatitis. To secure the best results ½ grain (0.03 gm.) of emetin hydrochlorid should be given hypodermically twice a day, or 1 grain (0.065 gm. ) once a day, for ten days or two weeks. If colic or severe diarrhea supervenes it may be checked by opium and bismuth subcarbonate. Once in four or five days the bowels should be cleansed by a saline purge and during the treatment the patient should remain in bed. After the disappearance of all symptoms, a stool obtained by the use of a saline cathartic should be examined once a month for several months and if amebæ are found the treatment should be repeated. Some observers have found that relapse is less likely to occur if ipecacuanha, 30 to 60 grains (2.0 to 4.0 gm.), in salol-coated pills, is given daily for several days after the discontinuance of the emetin. To prevent vomiting, the drug should be taken at bedtime, half an hour after a 15-minim dose (1 mil) of laudanum. Both emetin and crude ipecac often prove ineffectual in extremely acute and extremely chronic cases of amebiasis. In such cases, as well as in carriers, emetin-bismuth iodid, although it has some tendency to produce vomiting and diarrhea, is often of service. The usual dose is 2 to 3 grains (0.13–0.2 gm.) in salol-coated pills or in capsules, once daily, preferably after the mid-day meal for 10 or 12 successive days.

Irrigation of the bowel is frequently efficacious in chronic cases. It should be done once a day by means of a fountain-syringe and a long rectal tube, and with the patient in the knee-chest position or on his back with his hips well elevated. The best solution for the purpose is one of quinin bisulphate (1 to 5000 gradually increased to 1 to 1000) or one of silver nitrate (1 to 2000 gradually increased to 1 to 1000). From 1 liter to 2 liters should be allowed to enter slowly and the enema should be retained if possible ten or fifteen minutes. If the rectum is very irritable a small quantity of cocain solution (4 per cent.) may be introduced first. In intractable cases recourse may be had to colostomy or appendicostomy and irrigation of the colon through the wound.

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## CILIATE AND FLAGELLATE DYSENTERIES

Among the ciliated protozoan parasites capable of causing dysentery, the most important is *Balantidium coli*. This organism is an oval body, from 60 to 200 microns long and 50 to 70 microns wide, pointed at one end, and covered with parallel rows of cilia. Man is probably infected through water or food that has been contaminated with the fecal matter of hogs afflicted with the disease. Balantidial dysentery (balantidiasis) occurs frequently in the Philippine Islands and Japan, and isolated cases have been reported from nearly every country, including the United States. The parasite penetrates the submucosa of the large intestine and produces lesions and symptoms similar to those of amebic dysentery. In some cases it occurs in association with *Entamœba histolytica*. In chronic cases severe anemia

[1] Brit. Med. Jour., 1912, i, 1424.

simulating pernicious anemia may develop (Jennings, Logan[1]). The *diagnosis* is made only by finding the balantidia in the feces. Repeated search may be necessary, as in some cases the organisms are passed only at irregular intervals. The *prognosis* is grave, especially in advanced cases. As there is no specific *treatment*, reliance must be placed upon rest in bed, liquid diet, and active purgation with salines. Rectal irrigations with quinin (1 to 3,000 increased to 1 to 1,000) and methylene blue (1 to 1,000) have been recommended.

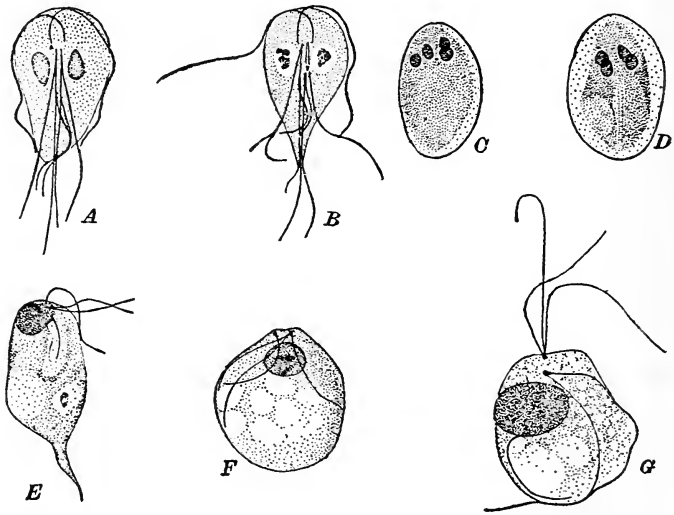


FIG. 5.—*A* and *B*, Lamblia intestinalis, active forms; *C* and *D*, cysts of same; *E* and *F*, Macrostoma mesnili; *G*, Trichomonas hominis. × 2000. (*After Ledingham and Penfol in "British Medical Journal."*)

At least two flagellates seem capable of setting up chronic diarrhea or even the true dysenteric syndrome, namely, *Lamblia intestinalis* and *Trichomonas hominis*. The infection may be pure or mixed with amebæ, balantidia, or other intestinal parasites. The method of transmission is not definitely known. *Lamblia intestinalis* is a pear-shaped organism, 10 to 20 microns long and 5 to 10 microns broad, with a saucer-like depression (cytostoma), on one side, four pairs of flagella, two axial rods and two nuclei. The cysts, which are frequently present in the stools when no active forms can be found, are slightly smaller ovoid bodies with four nuclei. *Trichomonas hominis* is also usually pear-shaped, but may be distinguished by its jerky irregular movements, and by the conspicuous undulating membrane running along one side. Cysts have not yet been observed.

The insoluble salts of bismuth, intestinal antiseptics, and ipecac are the remedies usually recommended for flagellate dysentery. French clinicians speak favorably of turpentine. Enemas of organic silver salts may also be of value.

[1] Amer. Jour. Med. Sci., Nov., 1921.

## RELAPSING FEVER

(Recurring Fever; Famine Fever; African Tick Fever)

**Definition.**—The term relapsing fever is applied to a group of acute, specific, infectious, and usually epidemic diseases, caused by certain species of spirochætæ, and characterized by alternating periods of fever and of apyrexia, each lasting, as a rule, from 5 to 7 days.

**Etiology.**—Relapsing fever prevails extensively at times in Europe, especially in Russia, Turkey, and the Balkan states, in India and China, and in various parts of Africa. It has been reported also from Central and South America. It was last epidemic in the United States in New York and Philadelphia in 1869. Age and sex are without special etiologic significance, although owing to greater exposure to infection males between 15 and 30 years furnish the majority of cases. Insanitary conditions favor the spread of the disease and not uncommonly an outbreak is preceded or followed by one of typhus. One attack usually confers temporary immunity lasting for several months.

The organism responsible for relapsing fever varies somewhat in morphologic and cultural characteristics in different countries, and, moreover, different insects are apparently concerned in transmitting the infection. Thus, the European fever is due to *Spirochæta recurrentis* (*Spirillum obermeieri*), which is probably transmitted by lice, although bedbugs have been frequently incriminated; the relapsing fever of East and West Africa is caused by *S. duttoni*, which is transmitted by a tick (*Ornithodorus moubata*); that of Northern Africa is caused by *S. berbera*, which is transmitted by lice, and that of India is due to *S. carteri* which is probably also carried by lice, although the evidence is not yet conclusive. Other species of spirochætæ have also been reported, as *S. novyi* for American and *S. persica* for Persian relapsing fever. The parasites, which are found in the patient's blood only during the febrile periods, are delicate actively motile, fiber-like spirals, measuring in length several times the diameter of a red blood-cell. Nothing is definitely known of their life history. In the case of *S. duttoni*, the infection may be transmitted by the tick to its own progeny (Leishman). It is noteworthy that the disease may be conveyed from one person to another also by direct inoculation of blood and that accidental infection in the laboratory has sometimes occurred.

**Morbid Anatomy.**—There are no characteristic lesions. The spleen is enlarged and soft. The liver, kidneys and heart show cloudy swelling. Infarction of the spleen and pneumonic consolidation of the lungs may sometimes be noted.

**Symptoms.**—After a period of incubation of from 3 to 10 days the disease sets in abruptly with a chill, headache, general neuromuscular pains, fever, and sometimes vomiting. The face is flushed, the tongue is heavily coated, the bowels are usually constipated and sometimes herpes is noted. The temperature reaches a maximum of 104° F. or more in 24 or 36 hours and then remains stationary with slight morning remissions for a period of from 5 to 7 days, when it falls by crisis, profuse sweating or a diarrhea usually marking the febrile recession. After an intermission lasting about a week, in which the patient feels much better or, perhaps almost entirely well, the febrile attack with its accompanying symptoms is repeated. Convalescence begins, as a rule, at the end of the second paroxysm, but it may be delayed until the close of the third or fourth. It is usually slow. In some cases, especially of the Asiatic type, there is no relapse. During the febrile period the spleen and liver are enlarged, the urine is scanty and often slightly albumin-

ous, and the blood shows numerous spirochætæ and a moderate polymorphonuclear leucocytosis. Insomnia is a striking feature in many cases, but delirium is unusual, except in very severe attacks. Jaundice is not infrequent in some outbreaks and occasionally there is a petechial eruption. Bronchial catarrh is sometimes noted in the first paroxysm.

*Complications* are not common. Pneumonia is the most frequent, but hemorrhages from the stomach, intestines or kidneys, colitis, acute nephritis and peripheral neuritis may occur. Ophthalmia has been observed as a sequel in some epidemics.

**Diagnosis.**—The characteristic febrile paroxysms with long intermissions and the presence of the spirochætæ in the blood are the distinctive features. The blood is infectious to susceptible animals (monkeys, mice, white rats) even during the apyrexial intervals, when it is apparently spirochete free. *Dengue* may be differentiated by the severe post-orbital pains, the absence of leucocytosis, the absence of spirochætæ, and the occurrence of a definite macular eruption. *Yellow fever*, which has several features in common with relapsing fever, may be recognized by the slowing of the pulse with the increasing temperature, the early albuminuria (second day) and the absence of splenic enlargement, of leucocytosis, and of the large distinctive spirochætæ. In *typhus fever* the pyrexial paroxysm is of longer duration and is not repeated, a dark macular eruption occurs on the 4th or 5th day, nervous symptoms are marked and spirochætæ are lacking. Considerable difficulty may be experienced at times in distinguishing between *Weil's disease* (*infectious jaundice*) and relapsing fever, as both are spirochetal infections. In Weil's disease, however, the temperature is quite irregular and jaundice is a constant feature. Guinea pigs are refactory to relapsing fever, but very susceptible to Weil's disease. Irregular forms of *malaria* may be distinguished by the course of the fever and the results of the blood examination.

**Prognosis.**—The prognosis is usually favorable, except in the severe but comparatively rare forms in which jaundice and hemorrhages are present. In old persons, however, fatal collapse sometimes occurs at the time of crisis even in cases that have been apparently mild. The average mortality is probably not above 6 per cent.

**Treatment.**—The prevention of the disease is based upon personal and domestic cleanliness and the avoidance and destruction of lice, bedbugs and ticks. As to treatment, arsphenamin or neoarsphenamin is virtually a specific. In debilitated subjects the initial dose should not exceed 6 grains (0.4 gm.). Complete rest, good nursing and an appropriate diet will do much to avert complications. Apart from the use of the specific, treatment is symptomatic. The pains may be controlled by acetphenetidin or aspirin, or, if necessary, by morphin hypodermically, and the high temperature by cold sponging.

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## TRYPANOSOMIASIS

Trypanosomiasis is the name applied to a group of diseases caused by infection with species of flagellated protozo abelonging to the genus Trypanosoma. Various kinds of animals, including man, are affected, and insects, especially certain species of biting flies, serve as intermediate hosts for the parasites. Of the trypanosomes known to be pathogenic for man the most important are *Trypanosoma gambiense* and *Trypanosoma rhodesiense*, which

cause the sleeping sickness of Africa. In Brazil there is a rare form of trypanosomiasis, which is due to *Schizotrypanum cruzi* and spread by a bug, *Lamus megistus*. In infants it is usually acute and characterized by fever, enlargement of the lymph-nodes, spleen, and thyroid gland and a kind of myxedematous condition. Death may occur with meningo-encephalitic symptoms, or the attack may pass into a chronic phase. In adults the disease is usually chronic and marked by enlargement of the thyroid gland, muscular weakness, cutaneous pigmentation and signs of hypothyroidism. Various nervous disturbances and cardiac irregularities may also occur.

Among trypanosomes pathogenic for animals but harmless for man are *T. brucei*, causing Magana, a disease very fatal among horses and other domestic animals in Africa; *T evansi*, causing surra, a disease among domestic animals in India; and *T. equiperdum*, causing dourine, a disease of horses in Africa, parts of Europe, and the United States.

## SLEEPING SICKNESS

### (Human Trypanosomiasis of Africa)

**Etiology.**—Sleeping sickness is caused by *Trypanosoma gambiense* and *Trypanosoma rhodesiense*, which are conveyed from man to man or from wild or domestic animals to man by the bites of the tsetse flies, *Glossina palpalis* and *Glossina morsitans*, respectively, the insects acting as intermediate hosts for the trypanosomes in much the same way as the mosquito does for the malarial organisms. As found in the blood, the parasite is an active spindle-shaped body, from 15 to 30 $\mu$ long, and provided with a macronucleus and micronucleus, a transparent undulating membrane along one side, and a single terminal flagellum. The disease is confined chiefly to Western and Central Africa, and although patients have frequently introduced it into other countries, they seem never to have disseminated it outside of the endemic regions.

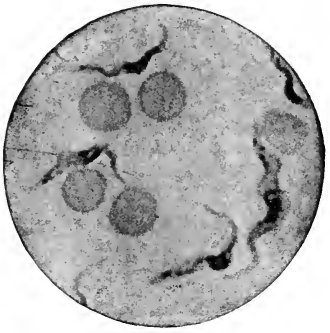

FIG. 6.—Trypanosoma gambiense. The parasite of sleeping sickness. × about 1400. (*Bulletin No. 1, Office of the Surgeon General, Washington, January*, 1913.)

**Morbid Anatomy.**—The characteristic lesions are chronic polyadenitis and chronic imflammation of the lymphatics of the central nervous system, with secondary meningo-encephalitis and, to a less extent, meningo-myelitis. The important feature microscopically is a perivascular infiltration of small round cells in the pia-arachnoid, especially about the pons and medulla.

**Symptoms.**—The disease is divided into two stages, known respectively as trypanosoma fever (Gambia fever) and sleeping sickness. The first stage, which follows a period of incubation lasting probably 2 or 3 weeks, is characterized by recurrent attacks of fever, painless enlargement of the lymph-nodes, especially those of the posterior cervical triangle, and the presence of trypanosomes in the blood and in juice obtained from the lymph-nodes by puncture. Patches of erythema or of edema, enlargement of the spleen, slight anemia, and mental hebetude are also observed in many cases.

The febrile paroxysms usually last about a week and reappear at intervals of a few days to several weeks.

After continuing for weeks, months, or, in some cases, as long as 2 or 3 years, the first stage merges into the second, that of sleeping sickness. This stage is marked by the appearance of the parasites in the cerebrospinal fluid, increasing weakness and lethargy, a peculiar apathetic expression, a low monotonous voice, tremor of the tongue and sometimes of the lips and hands, a shuffling gait, an evening rise of temperature (100° to 102° F.) a rapid feeble pulse, and drowsiness, gradually deepening into stupor and coma. As the end approaches the patient becomes helpless and emaciated, the temperature falls below normal, and the urine and feces are passed involuntarily. The fatal event in many cases is determined by bacterial infection in the form of pneumonia, ileocolitis, or purulent meningitis. The secondary stage usually lasts from a few months to a year.

**Diagnosis.**—In endemic areas the general symptoms are usually sufficient to arouse suspicion. The only positive proof of infection, however, is the finding of the trypanosomes in the blood, in juice withdrawn from the lymph-nodes, or in the cerebrospinal fluid.

**Prognosis.**—The outlook is extremely grave and after the second stage has been reached the disease is nearly always fatal.

**Prophylaxis and Treatment.**—Removal of plant and tree growth from the shores of lakes and rivers, destruction of wild game that serve as "reservoirs" for the parasites, isolation of infected persons, and protection by leggings, etc., of persons who must go about in infected districts have been suggested as prophylactic measures. With regard to treatment, encouraging results have been obtained from the use of atoxyl and sodiotartrate of antimony. Atoxyl may be given subcutaneously in doses of 2 or 3 grains (0.13–0.2 gm.) thrice weekly for two or three weeks, and followed by sodiotartrate of antimony, 1½ grains (0.09 gm.) of the drug in 3 pints (1.5 L.) of water being given by mouth daily, or ⅛ to ¼ grain (0.008–0.016 gm.) being given intravenously every day for two weeks. After an interval of three weeks the course of treatment should be repeated. Removal from infected regions is always advisable.

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## THE LEISHMANIASES

The protozoan parasites first described by Leishman and Donovan in 1903 are responsible for at least two affections, namely, *Kala-azar* (visceral leishmaniasis) and *Oriental sore* (cutaneous leishmaniasis). Infantile kala-azar is probably identical with the adult form, and not a distinct variety of leishmaniasis as was formerly believed.

### KALA-AZAR

**(Dum-dum Fever; Tropical Splenomegaly; Ponos)**

Kala-azar has been reported most frequently from India, especially from Assam, but it occurs in many other parts of the Orient, as well as in the Sudan and the Mediterranean littoral. The disease tends to spread along the routes of travel and after prevailing in a given region for a few years tends gradually to disappear. Sporadic cases, however, are common. A family incidence is frequently observed. The infection is apparently transmitted by a non-flying insect, and the bedbug has been especially incriminated.

The causal parasite, *Leishmania donovani*, as it occurs in man, is a nonflagellated ovoid body, measuring 2 by 3 microns, with a macronucleus, which is peripherally placed, and a micronucleus, which is often rod-shaped and set at a tangent to the macronucleus. It is found most frequently in the endothelial cells of the bloodvessels and lymphatics, and can almost always be obtained by puncture of the spleen, a procedure, however, which is distinctly dangerous. In a large proportion of cases it may also be detected in the peripheral blood, being found chiefly within the white corpuscles. In certain insects and in citrated culture media the organism becomes flagellated. The infantile type of kala-azar, which occurs chiefly in countries bordering on the Mediterranean, has been ascribed to *L. infantum*, but this parasite is now believed to be identical with *L. donovani*.

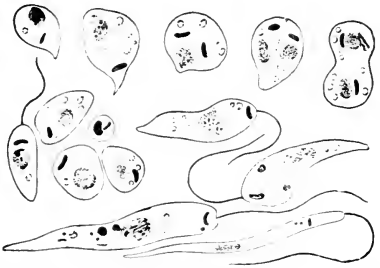

FIG. 7.—Leishmania donovani. Flagellated forms as seen in artificial cultures. (*After Leishman in Brumpt.*)

**Symptoms.**—The period of incubation is not definitely known, but according to Manson, it may be as short as ten days. The onset of the disease is usually with rigors, vomiting, irregular fever, (101°–104° F.) and enlargement of the spleen and liver, especially of the former. The fever, which is usually of a remittent type, with a double rise in the 24 hours, subsides in from 2 to 6 weeks, but is very prone to recur at varying intervals. The spleen rapidly enlarges and at the end of 3 months may reach to the umbilicus. The liver enlarges more slowly than the spleen, but eventually it may attain a considerable size and become cirrhotic, causing ascites. As the disease progresses, debility, emaciation and anemia become marked, the skin acquires a peculiar dark color (black fever), hemorrhages occur into the skin, and dropsical effusions make their appearance. In addition to the anemia of the later stages the blood throughout shows a pronounced leucopenia, with a relative increase of the large mononuclear forms. The duration of the disease is from 6 months to 2 years. At least 75 per cent. of the cases terminate fatally, death being due to exhaustion, or, more frequently, to some intercurrent affection, such as pneumonia, colitis, cancrum oris, and septicemia.

The **diagnosis** is based upon the irregular fever, marked splenomegaly, progressive anemia and emaciation, together with the leucopenia and the finding of the leishman bodies in the blood or in the spleen or liver juice. The diseases most likely to come into question are malaria, typhoid fever, malta fever and leukemia.

**Treatment.**—Prophylaxis consists chiefly in avoiding infected houses and in employing measures against the bedbug. In the treatment of the disease

favorable results have been reported from intravenous injections of tartar emetic—8 min. (0.5 mil) of a 2 per cent. solution every 2 or 3 days up to tolerance—50 to 60 min. (3.0–4.0 mils). Manson has found atoxyl useful. Quinin in doses of 60 to 70 gr. (4.0–4.6 gm.) daily has also been recommended (Rogers). Removal from infected regions is advisable.

## ORIENTAL SORE

**(Delhi Boil; Aleppo Boil; Espundia; Uta; Forest Yaws)**

Oriental sore is a specific ulcerating granuloma of the skin occurring endemically in Northern Africa, Asia Minor, Persia and India, and to a certain extent in Central and South America. It is cutaneous leishmaniasis, due to *Leishmania tropica*, which is virtually identical with *Leishmania donovani* causing Kala-azar. Infection may be direct or through the bite of an insect.

**Symptoms.**—In from a few days to two months after inoculation, a dull red papule appears, which gradually enlarges and becomes covered with fine scales and later with a yellowish crust. After 3 or 4 months the center of the papule breaks down forming an indolent, irregularly shaped, sharply cut, painless ulcer, which sometimes attains a diameter of several centimeters. In from a few months to a year healing begins, the resulting cicatrix often causing considerable deformity. The ulcers may be single or multiple and the areas attacked are usually the uncovered parts. Constitutional symptoms are absent, but in the South American variety ulcers may appear also on the nasal or buccal mucosa. As a rule, infection confers lasting immunity. The diagnosis is made definitely by finding the Leishmania in scrapings from the ulcer.

The internal **treatment** is the same as that of kala-azar. Locally caustics, especially carbon dioxide snow, have been used with some success.

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## ACUTE INFECTIOUS JAUNDICE

**(Weil's Disease; Spirochætosis Icterohæmorrhagica)**

These terms are applied to an acute infectious disease, commonly epidemic, and characterized by fever, jaundice, muscular and abdominal pains, marked albuminuria, and a tendency to hemorrhages.

The disease which was first described by Weil[1] in 1886, has appeared from time to time in various parts of the world. Japan has frequently been visited. A few endemic cases have been reported in the United States. In the recent European war outbreaks were common among the soldiers in Flanders and at Salonica. Men working in mines, rice fields, sewers, and trenches furnish the greatest number of cases. The specific etiologic factor is the delicate spiral-shaped parasite, Spirochæta icterohemorrhagiæ, isolated by Inada[2] and his associates. This organism is present in the blood during the first stage of the disease and in the urine after ten to fourteen days. Ido and Hoki[3] have shown that the rat is an active carrier of S. icterohemorrhagiæ and it has been suggested that this animal spreads the infection by means of

[1] Deutsch. Arch. f. klin. Med., 1886, 39, 209.
[2] Jour. Exp. Med., 1916, 23.
[3] Jour. Exp. Med., 1917, 26.

its urine. The disease is also transferable from man to man and from man to animals by direct blood inoculation. Among the lower animals the guinea pig is especially susceptible. One attack of infectious jaundice confers a certain degree of immunity.

**Symptoms.**—The onset may be sudden with a chill or gradual with headache, abdominal pain, and vomiting. An irregular fever (102°–104° F.) develops, intense aching in the muscles is complained of, and jaundice, usually moderate in degree, appears in from 3 to 5 days. The liver is, as a rule, enlarged, but the spleen is usually unchanged, the urine is albuminous and usually contains a variety of tube casts, and the blood shows a moderate leucocytosis. Prostration is almost always pronounced, hemorrhages into the skin and from the mucous membranes not rarely occur, and in severe cases delirium and the typhoid state may supervene. The fever continues for a few days or a week and then gradually subsides. Recovery usually ensues, but relapses are not infrequent, and convalescence is likely to be slow. Nephritis, iritis, optic neuritis and various psychoses have been reported as sequels. In European outbreaks the mortality has not often exceeded 3 or 4 per cent., but in Japan it has been as high as 38 per cent. In the diagnosis relapsing fever, yellow fever, bilious remittent fever, and other forms of infectious or toxic jaundice must be considered.

**Treatment.**—Assuming that the natural habitat of S. icterohemorrhagiæ is the rat, the extermination of this animal is, of course, an important prophylactic measure. The outlook for the production of a protective and curative serum seems to be good. As in other spirochetal infections arsphenamin appears to be of value.

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## YAWS

### (Frambesia)

Yaws is a chronic infectious, highly contagious disease, caused by *Spirochæta pertenue*, and characterized by a papular outbreak which tends to form cauliflower- or raspberry-like patches. The disease is a distinct entity, although it is closely related to syphilis.

Yaws is confined to tropical countries, occurring especially in the Philippines, Samoa, Fiji and many other islands of the Pacific, in Central Africa and in the West Indies. It is observed chiefly in children and apparently shows a predilection for the black and colored races. It is neither hereditary nor congenital, but is transmitted by direct contact, by means of fomites, and probably also by means of insects. An abrasion of the skin, however, is requisite for infection. The infecting parasite, *Spirochæta pertenue*, closely resembles the spirochæta of syphilis.

**Symptoms.**—The period of incubation, which usually lasts from 2 to 5 weeks, is frequently marked by an irregular fever, headache, muscular pains and digestive disturbances. Following these prodromal symptoms there may or may not be a primary lesion consisting of a small conical papule, which in a few days cracks at its summit, exudes sero-pus, and then dries up or, more frequently, develops into a mass of exuberant granulations bearing some resemblance to a raspberry (frambœsia). The primary lesion, which sometimes attains a diameter of several centimeters, is almost invariably extragenital. In from 1 to 3 months after the appearance of the pri-

mary yaw, which may have healed, but which more often is still present, constitutional symptoms again develop and are soon followed by the occurrence of a secondary eruption, which is more or less general and which has the same appearance as the initial lesion. The favorite seats of the eruption are the face and limbs, the genital region, and the parts around the natural orifices. The secondary stage usually lasts from 3 to 12 months, but in some cases the yaws continue to appear in successive crops over a period of years.

Following the secondary stage there are sometimes tertiary manifestations consisting of extensive ulcerations, often resulting in serious deformity. Periostitis, dactylitis, etc. are sometimes observed. Castellani has also described lesions analogous to the gummata of syphilis. Gangosa, or rhinopharyngitis mutilans, is regarded by some observers as a form of tertiary yaws.

**Diagnosis.**—The resemblance to syphilis is sometimes close, not only in the appearance of the lesions, but also in the occurrence of a positive Wassermann reaction. In yaws, however, children are especially attacked, although the disease is never congenital; the initial lesion is almost invariably extragenital; the secondary eruption is monomorphic; mucous patches and alopecia are wanting, and the viscera and central nervous system are not involved.

*Prognosis and Treatment.*—Recovery is the rule, if death occurs it is almost always the result of an intercurrent disease. Arsphenamin is specific and even more effective in yaws than in syphilis. Potassium iodid and mercury are also of service. Tonics are often required.

# INFECTIONS DUE TO FILTERABLE VIRUSES OR OF DOUBTFUL ETIOLOGY

## SCARLET FEVER

(Scarlatina)

**Definition.**—Scarlet fever is an acute, specific, infectious, and highly contagious disease, characterized by high fever, sore throat, a diffuse punctate erythematous rash, and a marked tendency to nephritis and suppurative otitis media.

**Etiology.**—The disease is endemic in almost all large cities, although the degree of its prevalence varies considerably in different localities. From time to time it attains epidemic proportions, autumn and winter being the seasons in which extensive outbreaks are most likely to occur.

The specific cause of scarlet fever is not known. Hemolytic streptococci are rarely absent from the throat of infected persons and are chiefly responsible for the complications of the disease, but they are apparently only secondary invaders, holding the same relation to scarlet fever that they frequently do to diphtheria and smallpox. The morbific agent, whatever it may be, has its chief source in the nasopharyngeal secretions and the discharges from suppurating ears. The accumulated testimony of recent years is opposed to the view that there is any connection between scarlatinal desquamation of the skin and infectivity. The inciting agent enters the body probably, as a rule, through the mouth and nose, although it is possible that there are other avenues of ingress. Scarlet fever is acquired in the majority of cases by direct contact with a patient who has the disease in its usual form, with a person who has mild and unrecognized scarlatina, with a convalescent, or with a healthy carrier. Mouth spray and hands contaminated with infected secretions are undoubtedly the most important agencies in conveying the disease. In some instances transmission is effected through the medium of clothing, toys, books, etc., that have been soiled with infected secretions or discharges. There is no convincing evidence that scarlet fever is ever airborne (Caiger, Goodall, Peters, Crooshank, Biernacki). In hospitals, persons who do not touch patients or come within range of droplets expelled from their noses or mouths very rarely acquire the disease. Outbreaks of scarlet fever have occasionally been traced to the use of milk that has been contaminated with buccal-pharyngeal secretions of infected persons or carriers. Transmission by direct inoculation has been shown to be possible (Strickler).[1] While the virus of scarlet fever is known to have considerable tenacity of life, instances of infection from clothing that has been stored in a trunk for years must be accepted with reserve.

Contagiousness is limited, but by no means lacking, at the onset of scarlet fever, most active during the eruptive period, and probably present so long as abnormal discharges occur from the upper air-passages, especially the nose. Infection lurking in the nose or post-nasal region is thought to play an important part in the production of so-called "return cases," that is cases of scarlet

[1] New York Med. Rec., 1899, lvi, 363.

fever in other children of a home to which a patient has returned after a stay in a hospital (Kemmshead,[1] Kerr[2]).

While no age is exempt from scarlet fever, the vast majority of cases (nearly 90 per cent.) occur in children between the ages of 1 and 15 years and about 50 per cent. of the cases between the ages of 3 and 8 years. Infants under 1 year are rarely attacked, and after puberty susceptibility gradually decreases, so that adults who have not had the disease in childhood usually escape altogether, and in this respect scarlet fever is in striking contrast to measles. The sexes as a whole show an equal receptivity to infection. Some families show a special proclivity to the disease, while others appear to be relatively immune. Negroes are less susceptible than whites, and among the Japanese and East Indians scarlet fever is said to be comparatively rare. Patients with wounds or burns and puerperal patients have been supposed to be especially prone to the disease but there is really no convincing evidence that this is the case. What has been termed surgical or puerperal scarlatina is usually a form of septic infection with an eruption resembling that of true scarlet fever, and when scarlet fever does occur in association with a wound or the puerperium it is probably merely a coincidence. The subject has been carefully reviewed by de Bovis,[3] Hamilton,[4] and Byers.[5] One attack of scarlet fever usually, but not invariably, protects from subsequent ones.

**Morbid Anatomy.**—The rash is not usually observed postmortem, except in hemorrhagic cases. Microscopic examination of the skin, however, may reveal an infiltration of the subcutaneous tissue and epidermis with polymorphonuclear leucocytes. The pharynx and tonsils exhibit inflammatory changes of varying intensity. False membrane is present in some cases. Areas of bronchopneumonia are not rarely found in the lungs. The liver, as in other acute infections, usually presents the changes characteristic of cloudy swelling and may be the seat of focal necroses. Non-specific degenerative changes also occur in the heart-muscle. The spleen is more or less swollen and on section shows enlargement of the Malpighian bodies. The kidneys are commonly the seat of inflammatory and degenerative changes. While the tubules are nearly always more or less affected, in the majority of cases the most conspicuous alterations are found in the glomeruli (glomerulonephritis) and consist of hemorrhage into the capsule, proliferation of the capsular epithelium and occlusion of the capillaries of the tuft by thrombi. In some instances neither the tubules nor the glomeruli are seriously affected, the chief lesion being an extensive accumulation of wandering cells, especially lymphocytes, between the tubules (acute interstitial nephritis). Enlargement of the lymph-nodes throughout the body was noted in all of the 21 cases of scarlatina examined by Pearce.[6]

**Symptoms.**—The *period* of *incubation* varies from 1 to 8 days, but it is usually from 2 to 4 days. The *onset* is sudden, generally with vomiting, sorethroat, headache and malaise. Vomiting occurs in at least three-fourths of the cases, but, as a rule, it does not persist for more than a day or two. In some instances the invasion is marked by chilliness or even a rigor, and occasionally in young children there is a convulsion.

The *temperature* rises rapidly, often attaining its maximum (103°–104° F.)

[1] Metropolitan Asylums Board. A Report of Return Cases of Scarlet Fever and Diphtheria. 1902.
[2] Textbook of Infectious Diseases, Oxford Med. Press, 1909.
[3] Semaine Méd., Jan. 29, 1902.
[4] Amer. Jour. Med. Sci., July, 1904.
[5] Brit. Med. Jour., Oct. 26, 1912.
[6] Med. and Surg. Rep. Boston City Hosp., 1899.

within 36 hours. It continues high, with but slight or moderate remissions, for 3 or 4 days, or until the eruption begins to fade, and then it gradually declines, usually taking 2 or 3 days to reach the normal. The average duration of the febrile period is from 7 to 9 days. Very mild attacks of scarlet fever are occasionally almost apyretic. The pulse is accelerated (130–140), often out of proportion to the elevation of temperature.

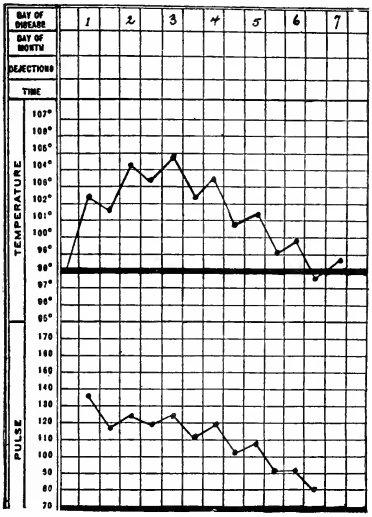


FIG. 8.—Temperature and pulse record of an ordinary case of scarlatina.

Early in the disease the *throat* becomes inflamed, inspection revealing redness and more or less swelling of the palate, uvula and tonsils. Not rarely the characteristic punctate rash is present on the soft palate and adjacent parts before any eruption is discernible on the skin. In well-marked cases the tonsils are considerably enlarged and exhibit small spots of creamy exudation in the crypts. In some instances the affected parts are covered here and there with thin loosely attached false membrane. The facial inflammation is accompanied by pain on swallowing, tenderness behind the angles of the jaw, and enlargement of the cervical lymph-nodes. The tongue, which at first is covered with a white fur, soon becomes denuded and after the third or fourth day presents a bright red surface studded with swollen papillæ. This so-called "strawberry" or "raspberry" appearance of the tongue is rarely absent, and while not pathognomonic of scarlet fever, has considerable diagnostic significance.

The *eruption* usually develops in from 12 to 36 hours after the onset. As a rule, it appears first on the sides of the neck and upper part of the chest, and then spreads rapidly to other parts, sometimes covering the whole body. It is essentially an erythema, usually of a bright red color, but at times of dusky red or even a purplish hue. Close inspection reveals a diffuse red surface closely set with minute darker red points. This punctation is especially

noticeable in the axillary regions and on the inner side of the thighs. Not infrequently the exanthem presents numerous pin-head sized papules which impart to the fingers a sensation of roughness similar to that observed in the condition known as goose-flesh. In other cases many miliary vesicles are seen in addition to the minute papular elevations (*Scarlatina miliaris*). The efflorescence disappears on pressure of the fingers, but reappears immediately when the pressure is removed. The skin of the affected parts is tense, and at times slightly swollen. Itching is often marked. The face, although deeply flushed, sometimes remains free from the punctiform rash, and even when it is invaded, the region around the mouth frequently escapes and so contrasts strongly with the reddened cheeks.

The eruption begins to fade, as a rule, about the third or fourth day and has mostly disappeared at the end of week. Coincident with its disappearance, *desquamation of the cuticle* occurs, the neck and chest being first affected. The exfoliation starts at many points and spreads centrifugally, thus forming irregularly rounded patches with ragged margins—a configuration somewhat characteristic of the disease. Except where the skin is thin, the scales are of considerable size. Indeed, on the back the epidermis may peel off in large sheets and on the hands and feet it may separate in the form of more or less complete casts. In rare instances, even the hair and nails are shed. Desquamation is usually completed in 2 or 3 weeks, but sometimes 6 or 7 weeks pass before the palms and soles are entirely free. Occasionally a secondary desquamation follows the first.

With the exception of marked restlessness, *nervous symptoms* may be wanting. In the more severe cases, however, there is frequently somnolence and at night slight delirium. The *urine* during the febrile period is scanty and dark colored, and, even in the absence of actual nephritis, it may show a trace of albumin and a few blood cells and tube-casts. Examination of the *blood* reveals a well-marked polymorphonuclear leucocytosis (15,000–30,000), which usually attains its maximum at the acme of the rash. The *lymph-nodes* in the axillæ and groins, as well as those in cervical region, are almost always enlarged.

**Variations.**—No eruptive fever presents greater variations in its manifestations than scarlatina. In some instances there is almost no fever, the throat symptoms are extremely mild, the eruption is scanty, faint and transient, the child appears little, if at all, ill, and the nature of the case remains doubtful until desquamation occurs. Rarely the eruption is absent, or is so faint and evanescent that it is overlooked (*scarlatina sine eruptione*), and the only throat manifestation is a slight faucial and tonsillar congestion (*scarlatina sine angina*).

In other cases the throat is gravely affected (*scarlatina angiosa*). The lymph-nodes at the angle of the jaw and the cellular tissue of the neck are intensely swollen. False membrane appears early on the tonsils, palate and uvula. The nares become infected and emit an offensive purulent discharge. Suppuration of the middle ear almost always ensues. The mouth is opened with difficulty and there is marked dysphagia. The constitutional symptoms are severe, the temperature being high (104°–106° F.) and the general condition that of a profound septicemia. The cervical lymph-nodes frequently break down, and extensive sloughing of the tonsils or palate may occur. The majority of such cases end fatally, death being due to septicemia, bronchopneumonia, or edema of the larynx.

In the type known as *malignant scarlet fever*, which fortunately is now rare, the toxemia develops with great rapidity and is overwhelming. The temperature is high, sometimes reaching 106° or 107° F., vomiting is severe,

the patient becomes wildly delirious and then comatose, and death ensues within 24 or 36 hours, or before the occurrence of the eruption. If the fatal termination is delayed for two or three days and the rash appears, it is likely to be blotchy and livid and accompanied by numerous petechiæ. Hemorrhages from the mucous membranes may also occur.

**Complications.**—The most common complications of scarlet fever are the result of the oral and nasal sepsis. Infection frequently travels through the Eustachian tube to the tympanic cavity, producing *suppurative otitis media*. This complication occurs in from 10 to 15 per cent. of the cases and in about half of the number both ears are affected. Secondarily, necrosis of the mastoid bone, thrombosis of the lateral sinus, meningitis, cerebral abscess or facial palsy may ensue. Many deaf mutes owe their condition to scarlatina. Rhinitis is present in nearly all of the more severe cases of scarlet fever and not rarely it results in an *involvement of one or more of the accessory nasal sinues*. In from 10 to 15 per cent. of the cases the cervical adenitis ends in suppuration of the affected nodes and the formation of an *abscess*. Occasionally a *secondary adenitis* develops after all the symptoms have subsided and convalescence is apparently far advanced. Persistent fever after the disappearance of the eruption should always excite suspicion of a suppurative process in the ear, one of the sinuses or a lymph-node. Occasionally a *diffuse cervical cellulitis* supervenes, and if this lesion does not prove speedily fatal, extensive sloughing may ensue and sinuses form, or profuse hemorrhage may occur from one of the large vessels of the neck. Exceptionally, scarlatinal lymphadenitis becomes chronic, the affected nodes remaining large and brawny for many months after the attack. Bokai observed *retropharyngeal abscess* 7 times in 664 cases of scarlatina. *Perichondritis of the larynx* is an occasional complication. *Bronchopneumonia* is more frequent than is usually supposed. Hutinel[1] found that about one-third of the deaths in 2500 cases were from this cause. *Pleurisy*, usually purulent, may follow pneumonia or occur independently of it.

*Acute nephritis* varies in frequency in different epidemics. Excluding the cases in which there are no evidences of the disease other than a trace of albumin and a few tube-casts in the urine for a few days at the height of the infection, the average incidence is about 5 or 6 per cent. The disease usually develops in the period of desquamation, between the second and fourth weeks, and it may occur in the mildest cases. As a rule, the onset is signalized by a return of the fever, puffiness of the eyelids or anasarca, and a decrease in the quantity of urine, although exceptionally there may be for a time increased secretion. The urine is high-colored, acid in reaction, of high specific gravity and contains a large amount of albumin, numerous bloodcells, and a great variety of tube-casts. At times it is very bloody. In severe cases uremia may supervene with headache, vomiting, convulsions and coma. Sometimes the occurrence of nephritis is revealed only by the urinary changes, hence the importance of examining the urine at frequent intervals. Death may occur from uremia, edema of the lungs, effusion into the serous sacs, or acute heart failure, or chronic nephritis may supervene directly upon the acute attack or may develop after an intercurrent free period of many years duration. Complete recovery, however, frequently occurs, even after the development of severe uremic symptoms.

*Arthritis*, or so-called "scarlatinal rheumatism" is a somewhat frequent complication. Heuber[2] observed it in 8 per cent. of 338 cases; Baum[3]

[1] Arch. de Méd. des enf., 1916, xix, 57.
[2] Deutsche Klinik, 1902, vii, 286.
[3] Jour. Amer. Med. Assoc., Oct. 10, 1903.

in 3.6 per cent. of 628 cases; and Barasch[1] in 5.9 per cent. of 1438 cases. It usually develops about the time of desquamation and is characterized by tenderness and swelling in various joints, especially the wrists, phalanges and elbows. Suppuration of the joints rarely occurs. Smith and Sturge[2] saw it only 9 times in 5000 cases. *Endocarditis* and *pericarditis* are infrequent and occur chiefly in septic cases. *Myocarditis*, on the other hand, is fairly frequent and most of the circulatory disturbances of scarlet fever are referable to this lesion.

*Organic affections of the nervous system* are not common. As has already been stated meningitis, cerebral abscess, and facial palsy occasionally occur in connection with otitis media. A few cases of hemiplegia and of polyneuritis are on record. Priestley[3] observed 13 cases of chorea in 5355 cases of scarlet fever. Scarlet fever often coexists with other infections. In many of the severe cases *septicemia* or *septicopyemia*, usually of streptococcic nature, is present and it is the most frequent cause of death. The false membrane frequently seen on the throat in scarlet fever is usually due to the streptococcus but in a certain proportion of cases it is produced by the Klebs-Loeffler bacillus and signalizes the concurrence of *true diphtheria*. More rarely, scarlet fever is associated with chicken pox, measles, whooping cough or typhoid fever.

**Relapse and Recurrence.**—Relapse is rare. Griffith[4] observed it in 0.7 per cent. of 2000 cases; Sloan[5] in 1.8 per cent. of 14,143 cases, and McCollum[6] in 0.4 per cent. of 1000 cases. Recurrence of the disease a second time is even more rare than relapse, although persons who have had scarlet fever not infrequently develop angina when exposed again to infection.

**Diagnosis.**—In typical cases the diagnosis is easy. It is based on the sudden onset with sore throat and vomiting, the rapid rise of temperature, the disproportionate acceleration of the pulse, the early appearance of a punctiform erythematous rash, the enlargement of the cervical lymph-nodes and the peculiar appearance of the tongue. In *measles* there is much less tendency to vomiting, the catarrh affects chiefly the eyes, nose and bronchi, and scarcely at all the throat, the "strawberry tongue" is absent, the rash appears later (about the fourth day), is distinctly papular and blotchy, is surrounded in many places by areas of healthy skin, does not spare the region about the mouth, and is almost always preceded by an eruption of "Koplik's spots" on the buccal mucous membrane, and, finally, there is no leucocytosis.

In *rubella* the period of incubation is longer, the invasion is mild and without vomiting, the sore throat is slight and usually accompanied by catarrhal symptoms, the tongue lacks the strawberry appearance, and the rash appears first on the face, is fleeting, and ordinarily consists of discrete rose-red spots. Even when the eruption is scarlatiniform on the face and trunk it is usually macular and blotchy on the legs.

*Diphtheria* may cause confusion, as false membrane sometimes appears on the throat in scarlet fever and an erythema occasionally occurs on the skin in diphtheria. Moreover, the two diseases not rarely coexist in the same patient. In diphtheria, however, the false membrane is, as a rule, thick, of a grayish-white color and firmly adherent, diphtheria bacilli are present in the secretions of the throat, the "strawberry tongue" is absent,

[1] Deutsch. med. Woch., 1915, xli, 4.
[2] Brit. Med. Jour., Nov. 16, 1895.
[3] British Med. Jour., Sept., 1897.
[4] Quarterly Med. Jour., Oct., 1895.
[5] Lancet, 1903, i, 436.
[6] British Jour. of Dermatol., 1910, xxii, 309.

and if an exanthem develops it is transient and not often widespread or punctiform.

In *acute follicular tonsillitis* the onset is sudden and the temperature as high as in many cases of scarlet fever, but the tongue is not red and papillated, and if an erythema occurs, it is of limited distribution, transient, without punctation and not followed by desquamation.

*Erythema scarlatinoides* (*desquamative exfoliative dermatitis* is characterized by a diffuse, often punctiform, rash, more or less pyrexia and partial or complete desquamation of the cuticle and, therefore, may readily be confused with scarlet fever. In erythema scarlatidinoides, however, there may be a history of previous attacks, the invasion is mild and without vomiting, the tonsils and fauces are not swollen, although they may be slightly congested, the tongue is not characteristically altered, the cervical lymph-nodes are not enlarged, and the intensity of the rash is often out of all proportion to degree of constitutional disturbance.

*Septicemia* may produce an erythematous eruption suggestive of that of scarlatina, but in this condition there is usually evidence of local suppuration and the fauces and tonsils are not swollen. Certain *drugs*, such as quinin, belladonna, antipyrin, and antitoxic sera not rarely give rise to rashes resembling that of scarlatina, but such eruptions are rarely generalized and are usually accompanied by other symptoms referable to the action of the drug concerned, but not by fever, sore throat, adenitis, or the "strawberry tongue."

**Prognosis.**—The prognosis of scarlet fever is influenced by the severity of the prevailing epidemic and also by the age and the general condition of the patient. In some outbreaks the mortality has reached 30 per cent., while in others the cases have been so mild that scarcely a death has resulted. It is generally believed that the disease is of a milder character today than it was half a century or more ago. The fatality of scarlatina is greater among the poor than among the well-to-do, and infants are much more likely to succumb to the disease than older children. In 167,840 treated in the Hospitals of the Metropolitan Asylums Board during 13 years the mortality, according to Caiger,[1] was 4.3 per cent. In 11,216 cases reported in Philadelphia during 5 years the lethal rate, according to Graham,[2] was 5.4 per cent. An average mortality of 8.4 per cent. is given by McCollum[3] on the basis of over 37,810 cases in Boston, covering a period of 28 years. In 2,946 cases in the Riverside and Willard Parker Hospitals, N. Y., the death-rate was 8.5 per cent. (Fischer[4]). In 1438 cases in Berlin, analyzed by Barasch,[5] the mortality was 15 per cent. Kling and Widfelt[6] state that in Stockholm the mortality during the last 17 years has ranged from 1.45 to 8.63 per cent. About 90 per cent. of the deaths from scarlet fever occur in children under 10 years of age (Osler). In children under the age of 5 years the *mortality* is from 15 to 20 per cent.

In individual cases the outlook is serious in proportion to the severity of the anginose or the septic symptoms.

**Prophylaxis.**—Teachers and children who have been exposed to infection should be excluded from school for a week after the last known contact. No method of artificial immunization is available. The patient himself should be isolated at once. The sick-room should be large and airy, and, if possible,

[1] Allbutt and Rolleston, System of Medicine, 1906, II.
[2] Jour. Amer. Med. Assoc., Oct. 28, 1916.
[3] Quoted by Dublin, Jour. Amer. Med. Assoc., May 27, 1916.
[4] Jour. Amer. Med. Assoc., Dec. 28, 1907.
[5] Deutsch. med. Woch., 1915, xli, 4
[6] Hygiea, 1917, 79, No. 24.

located at the top of the house. All unnecessary furniture should be removed from the room and no one should be admitted to it except the physician and the nurse. All articles that have been in contact with the patient must be thoroughly disinfected before they are permitted to be taken to any other part of the house. Discharges from the nose, throat, and ear are best received on old muslin or linen and then destroyed by fire. Isolation should be continued for 6 weeks, or longer, if there is any discharge from the nose or ears, as it has been virtually established that so-called "return cases" are due rather to these abnormal secretions than to the desquamating epithelium *per se*.

When the period of quarantine is completed, the patient should be given a hot bath and well scrubbed with soap. He should then be dressed in clean underclothing and removed to another room. Finally, the sick-room should be thoroughly disinfected and cleaned, and then exposed to the air and sunlight for two or three days.

**Treatment.**—The treatment of scarlet fever is virtually symptomatic, for while a number of favorable reports on the use of *blood-serum* of patients convalescing from the disease have recently appeared (Landsteiner, Levaditi,[1] Zingher,[2] Weaver,[3] Kling and Widfelt[4]), the value of this remedy has not been fully demonstrated. From 30 to 90 mils of the serum are given intramuscularly, and repeated if necessary.

Rest in bed from the onset is imperative and should be continued for at least three weeks, even in the mildest cases. Milk, junket, koumiss, ice cream, gruels, toasted bread, and fruit-juices are suitable forms of nourishment. So as not to tax unnecessarily the kidneys, animal broths, with the exception of oyster or clam broth, should be withheld until convalescence is well established. Water should be given freely to relieve thirst and to keep the secretions active. The addition of an alkaline diuretic, such as potassium citrate, to the water serves a useful purpose. The bowels should be kept regular by mild saline aperients or cascara sagrada. Irrigation of the throat with normal salt solution or a 4 per cent. solution of boric acid is usually advisable if the *angina* is severe, but if the procedure meets with serious resistance it is better to dispense with it. In older children mild antiseptic gargles may be employed with advantage.

In many cases no special medication is required. Sponging with tepid water once or twice a day has a soothing effect. If the *vomiting* is severe it may be necessary to withhold food for a time and to administer cracked ice, bismuth subcarbonate, or cerium oxalate. *High temperature* (above 103.5° F.) is best controlled by cold sponge baths, cold packs, or graduated tub-baths (90° F. gradually reduced to 75° or 70° F.). In some cases with high fever and extreme restlessness immersion for ten minutes in water at 105° F. reduces the temperature and exerts a pronounced sedative effect. Antipyretic drugs should, as a rule, be avoided. Daily inunctions of the body with cold cream, cocoa butter, or carbolized oil serve to allay *itching*. When *restlessness*, *insomnia* and *delirium* are not relieved by cold applications to the head and the hydrotherapeutic measures already suggested, the use of chloral is advisable. From 2 to 3 grains (0.13–0.2 gm.) for a child of 2 to 4 years may be given in syrup of orange and water and repeated in two hours, if necessary. Sometimes a combination of a bromid and chloral acts better than the latter alone. A few small doses of phenacetin (2 grains,—0.13 gm.) may also prove efficacious.

[1] Ann. de l'inst. Pasteur, 1911, xxv, 754.
[2] Jour. Amer. Med. Assoc., 1915, lxv, 875.
[3] Jour. of Infect. Diseases, 1918, xxii, No. 3.
[4] Hygiea, 1917, lxxix, No. 24.

*Adenitis* is best treated by applying an ice-bag or cold compresses. An ointment of ichthyol (20 per cent.) has been recommended. When suppuration occurs the abscess should be opened and treated according to modern surgical practice.

*Otitis* should be sought for at frequent intervals, as in young children, especially, its occurrence is not always suggested by pain. In the cases in which earache develops, dry heat to the ear is sometimes effective; not rarely, however, it may be necessary to irrigate the ear with hot water and then to drop into it a solution of cocain (4 per cent.). Bulging of the tympanic membrane calls for incision and liberation of the pent-up pus.

*Arthritis* may be treated by wrapping the affected joints in cotton-wool, after first painting them with tincture of iodin, and by administering acetylsalicylic acid. *Circulatory weakness* will require the use of such drugs as digitalis, caffein, camphor, etc.

Should *nephritis* develop cupping (dry or wet) over the loins, followed by hot fomentations or poultices, often proves useful. Aperients, especially salines, are indicated. Warm baths, hot-packs or hot air baths should be used to promote diaphoresis, and alkaline diuretics (potassium citrate, potassium acetate or potassium bicarbonate) should be given to increase the urinary output.

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## MEASLES

(Rubeola; Morbilli)

**Definition.**—Measles is an acute, specific, infectious, and highly contagious disease, characterized by catarrh of the air-passages, moderate fever, and an eruption of slightly elevated red papules, which appears about the fourth day, lasts four or five days, and is followed by branny desquamation of the skin.

**Etiology.**—Measles is apparently the most contagious of the acute exanthemata and susceptibility to it is almost universal. It is communicable from the close of the period of incubation until a day or two after the disappearance of the rash, the height of its infectiousness probably being from the beginning of the catarrhal symptoms to the fall in temperature. The disease is endemic in all populous centers and from time to time it breaks out in epidemic form. The maximum intensity of epidemics is usually reached in the winter months.

Children between the ages of 1 and 10 years are the chief sufferers, but no age is exempt, and even the *fœtus in utero* may be attacked if the mother is the subject of the disease. As a rule, however, infants under six months of age escape. Adults who have not had measles in childhood almost always contract it when exposed to infection, individual immunity being uncommon. One attack of the disease usually protects from subsequent ones, recurrence, contrary to popular belief, being very rare.

The exciting cause of measles has not been determined. Tunnicliff[1] isolated a small anaërobic coccus from the blood in 42 of 50 cases, but his observations have not yet been confirmed. The specific virus, whatever its nature, is present in the nasopharyngeal secretions and in the blood.

The scales of the skin, however, seem to be harmless, unless they are

[1] Journ. Amer. Med. Assoc., April 7, 1917.

contaminated with the patient's secretions. Both the catarrhal secretions and the blood have been shown to be infective for monkeys (Anderson and Goldenberger[1]) but attempts to produce the disease in man by inoculation have not yielded conclusive results.

Measles is conveyed chiefly by direct or indirect contact. It is likely that air currents are important only in so far as they serve to distribute mouth spray and droplets of infected secretion and that they do not operate outside of a radius of about six feet. The transmission of the disease by third persons or fomites is rare, if it occurs at all.

**Morbid Anatomy.**—The usual signs of catarrhal inflammation are found in the conjunctiva, in the respiratory tract, and not rarely, also, in the alimentary canal. In the vast majority of cases the lungs are the seat of bronchopneumonia, and when cut open exhibit numerous discrete nodules of consolidation.

These nodules are of a grayish or yellowish color, raised above the cut surface, and distributed around the terminal bronchioles. The pneumonic process is probably always the result of secondary infection, the organism usually concerned being a hemolytic streptococcus. The lymph-nodes throughout the body, and, as a rule, the spleen, are more or less swollen.

**Symptoms.**—The *period* of *incubation* is from 7 to 14 days, with an average of about 11 days. As a rule, the health is not disturbed during this stage, although occasionally there is more or less lassitude. Leucopenia with a relative increase of the polymorphonuclear cells is often present.

The *invasion* is marked chiefly by catarrhal symptoms and moderate fever. Vomiting occasionally occurs, but it is very much less frequent than in scarlatina. Occasionally the onset is abrupt with chilliness or a convulsion. The *catarrh* affects the conjunctivæ and air passages and causes suffusion of the eyes, photophobia, lachrymation, sneezing, coryza, hoarseness and a hard, dry cough. A few coarse râles are often audible over the chest. The *fever* may develop abruptly or gradually. In many cases the *temperature* rises to 102° or 103° F. during the first day, sharply remits on the second or third day, then on the appearance of the rash rises again to 103° or even 104° F., and after remaining at this level for 2 or 3 days finally falls to normal by rapid lysis. In other instances the temperature rises gradually, until the eruption is fully developed, remains almost stationary for a day or two, and then makes a rapid descent. The pyrexia usually lasts in all about a week and is accompanied by frontal headache, furring of the tongue, anorexia, acceleration of the pulse, drowsiness, and irritability. The *urine* presents the usual febrile changes and occasionally contains a trace of albumin. The diazo-reaction is present in many cases at the height of the disease. The *blood-picture* is not altogether constant, but during the eruptive stage, it usually shows a pronounced hypoleucocytosis with a predominance of lymphocytes.

Although it had long been recognized that the mucous membrane of the mouth may show patchy redness in advance of the cutaneous exanthem, to Koplik[2] belongs the credit for having first accurately described the *buccal eruption* which is almost pathognomonic of measles and which in most instances precedes the cutaneous rash by one, two, or even three days. This exanthem consists of minute bluish-white specks surrounded by bright red areolæ, and is to be found especially on the mucous lining of the cheeks and lips. It is present in at least 90 per cent of the cases, but it is often visible only in bright daylight.

[1] Public Health Rep., June 9, 1911; Jour. Amer. Med. Assoc., Aug. 5, 1911.
[2] Archives of Pediatrics, Dec., 1896.

The *cutaneous eruption* usually appears between the third and the fourth day of the febrile period, and first shows itself behind the ears, on the neck, and on the forehead, whence it rapidly spreads to the face, trunk, arms and legs. It consists of small, slightly elevated, dusky red papules, with crenated margins and a soft velvety feel. At first the lesions are discrete and of a round or lenticular shape, but as they become more abundant they tend to group and form blotches with irregular edges and more or less crescentic outlines. These crescentic forms, with intervening islets of healthy skin, have considerable diagnostic significance. When the efflorescence is

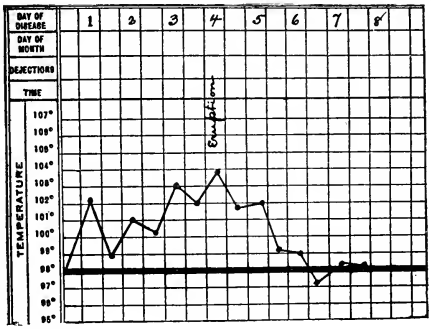


FIG. 9.—Temperature curve of an ordinary case of measles with pre-eruptive remission.

pronounced the face usually appears swollen and congested, especially about the eyes. Variations in the eruption are by no means uncommon. In some instances the spots are so numerous that they coalesce and form areas of uniform redness that closely resemble those of scarlet fever (*morbilli confluentes*); occasionally the papules are surmounted by pinpoint vesicles (*morbilli vesiculosi*); and in rare instances the true exanthem is preceded by a transient scarlatiniform erythema or a rosy macular eruption.

With the development of the rash the fever and catarrhal symptoms increase in severity and occasionally diarrhœa supervenes. After three or four days the eruption disappears leaving behind faint reddish stains which last a few days longer. In the week after the eruption *desquamation* occurs, the cuticle coming off in fine bran-like scales. With the fading of the rash the other symptoms rapidly subside and, unless some complication ensues, the patient is usually quite well at the end of ten days or two weeks from the onset.

**Variations.**—*Mild, abortive types* occur in which the temperature does not exceed 102° F., the catarrh is slight, the eruption is scanty and poorly developed, and convalescence is completed within a week. Again, there is a *malignant* or *fulminant type*, characterized by an abrupt and stormy onset, hyperpyrexia, pronounced nervous symptoms, and death from cardiac failure on the second or third day. The rash in such cases, if there has been time for it to appear, is often livid or actually pectechial.

*Hemorrhagic measles*, which is rare at the present time, occurs in two forms. In one, the hemorrhagic extravasations are confined to the papules and the disease, while severe, pursues the usual course. In the other form there is bleeding not only into the skin, but also from the mucous membranes,

the constitutional symptoms are severe, and death occurs in from two to five days. *Measles without eruption* (*morbilli sine exanthemate* and *measles without catarrh* (*morbilli sine catarrho*) are also described.

**Complications and Sequelæ.**—*Bronchopneumonia*, usually due to a hemolytic streptococcus, is the most common complication and is responsible for the large majority of deaths in the fatal cases. It is especially prone to attack poorly nourished children, although in camp epidemics of measles it frequently occurs in robust young men when streptococcus carriers are present. *Lobar pneumonia* is comparatively rare. *Laryngitis* with ulceration of the laryngeal cartilages or with formation of false membrane is occasionally observed. Theodore Fisher[1] has reported 4 cases of *bronchiectasis* following measles. The comparative frequency with which latent *tuberculosis* is reactivated by measles is emphasized by nearly all writers. According to Bushnell[2] of 5,945 cases of measles occurring among the American troops during the World War active tuberculosis developed in 2.91 per cent.

*Otitis media* is somewhat frequently observed, but it is usually of a milder type than when it occurs in scarlatina. *Ileocolitis* often develops at the height of the attack or during convalescence. *Endocarditis* and *nephritis* are rare complications. *Gangrene* of the cheek (noma) or vulva, while relatively rare, is apparently more common in measles than in any other acute infection. *Eye complications*—phlyctenular conjunctivitis, keratitis and marginal blepharitis—are sometimes observed. In 1912 Griscom[3] collected from the literature 23 cases of optic neuritis following measles. *Meningitis*, *myelitis*, and *peripheral neuritis* have occasionally been observed. Meningitis is usually of otitic origin or tuberculous. Möller[4] found it 5 times in 537 necropsies.

As Hebra first pointed out *recession* of the *eruption*, which sometimes occurs in measles, is the result, rather than the cause of certain internal complications, the spots fading from failure of the circulation. It is not unusual for measles to be complicated by other specific infections, such as *diphtheria*, *scarlet fever*, and *whooping cough*. Measles occurring during pregnancy usually results in *abortion* or *premature birth*.

**Relapse and Recurrence.**—Relapse is occasionally seen, but is rare. Undoubted instances of a second attack are also very rare.

**Diagnosis.**—*Rubella* is the disease which simulates measles most closely. In rubella, however, the prodromal stage is short, rarely more than 24 hours; the catarrhal symptoms are very mild; the fever does not often exceed 101° or 102° F. and is of short duration; Koplik's spots are absent, although a reddish macular eruption may be present on the buccal mucous membrane and over the soft palate; the rash is usually less dusky than that of measles, spreads very rapidly, shows little tendency to group and form crescentic blotches, and disappears, as a rule in from 1 to 3 days, often fading from the face and upper part of the trunk before it has reached the legs; and finally enlargement of the post-auricular and post-cervical lymph-nodes is usually more conspicuous than in measles. The differential diagnosis of measles from *scarlet fever* is considered on p. 224 and that of measles from smallpox on p. 239. Among other conditions that may resemble measles may be mentioned *secondary syphilis with a roseolar eruption*, *erythema multiforme*, and *certain drug rashes*, such as may be produced by antipyrin, capaiba, quinin, chloral and antitoxic sera.

[1] Lancet, Oct. 31, 1903.
[2] Jour. Amer. Med. Assoc., June 15, 1918.
[3] Annals of Ophthalmology, Jan., 1912.
[4] Wurzburg Thesis, July, 1896.

**Prognosis.**—The aggregate mortality from measles is high, about 9000 deaths from the disease occurring annually in the United States. The actual percentage of deaths, however, is comparatively low ranging from 1.5 to 10 per cent., with an average of about 3 or 4 per cent. Owing to a greater opportunity for cross-infection with streptococci the mortality rate is uniformly higher in foundling asylums, children's hospitals and military camps than in private practice. In large institutions the lethal rate has sometimes exceeded 30 per cent. Age is an important factor in cases occurring before puberty, more than one-half of the deaths being in children under 3 years and at least 90 per cent. in the first 6 years of life. Individuals who are constitutionally feeble or who are debilitated by preexisting disease also furnish many victims. On the other hand, very few fatal cases occur in private practice in robust children over the age of three years.

Death in the course of the disease is usually the result of bronchopneumonia, but it may be due to ileocolitis, to cross-infection with diphtheria or to meningitis. Even after recovery from measles itself, death may ensue from tuberculosis which has been reactivated by the superimposed infection.

**Prophylaxis.**—The patient should be isolated from the earliest possible moment until at least 5 days after the disappearance of the rash. All articles that are soiled with the patient's nasal or pharyngeal secretions should be disinfected. Exposed susceptible children should be kept from school and from all intercourse with other children from the sixth to the fourteenth day after contact, but they need not be sent from home. Adults and children who have previously had measles need not be restricted after being exposed to infection. Terminal disinfection, other than thorough cleaning of the sick-room, is unnecessary, as the virus is very short-lived.

The studies of Richardson and Connor, Degkwitz, McNeal[1] and others indicate that serum obtained from patients convalescing from measles between the seventh and fifteenth days after the disappearance of fever, if injected intramuscularly in susceptible children not later than the fourth day after exposure to infection, affords immunity lasting at least two months. The dose of the serum is 5 mils.

**Treatment.**—The sick-room should be well ventilated, but free from drafts, and kept at a temperature of about 70° F. Even in the absence of complications, it is advisable for the patient to remain in bed for at least 10 days from the onset. On account of the photophobia, bright light should be excluded from the room or the bed so placed that the patient's face will be directed away from the windows. Cough is lessened by keeping the atmosphere of the room somewhat moist. The diet should be light. In the case of infants the milk-mixture must be considerably diluted. For older children and adults, milk, junket, light broths, soft boiled eggs, and corn starch preparations are suitable forms of nourishment. Water should be proffered at frequent intervals. The fever is seldom sufficiently high to demand bathing, but a tepid sponge bath once a day is requisite. Hot baths and hot drinks are indicated when the rash is delayed. If there is much itching, cold cream or olive oil may be applied to the skin after it has been bathed and dried.

Constipation is best relieved by enemas or glycerin suppositories. Irritation of the eyes is benefited by frequent applications of a 3 per cent. solution of boric acid. When the conjunctivitis is severe the eyes should be protected by dark glasses.

Cough is the symptom that most frequently requires attention. Such a mixture as the following is often useful:

[1] Jour. Amer. Med. Assoc., Feb. 4, 1922.

℞. Potassii citratis..... ʒii (8.0 gm.)
Tincturæ opii camphoratæ..... fʒii–iv (8.0–15.0 mils)
Tincturæ belladonnæ..... ♏xl (2.5 mils)
Glycerini..... fʒii (8.0 mils)
Aquæ..... q. s. ad fʒiii (90.0 mils) M.
Sig.—A teaspoonful every two or three hours for a child of four years.

When the bronchitis is severe, mild sinapisms may be applied to the chest with advantage. Diarrhea usually yields to bismuth subcarbonate, with or without opium. Pronounced nervous symptoms are best treated by warm tub-baths and the administration of appropriate doses of a bromid. The ears should be examined frequently, even in the absence of earache. When pus is detected it should be evacuated at once by free incision of the tympanic membrane.

During convalescence tonics—iron, strychnin, arsenic and cod-liver oil—are frequently indicated.

## RUBELLA

(Rötheln; German Measles; Epidemic Roseola)

**Definition.**—Rubella is an acute, specific, infectious, and highly contagious disease of short duration, characterized by a red maculopapular eruption, slight fever, mild catarrhal symptoms, and almost complete freedom from complications. Although it resembles measles on the one hand and scarlet fever on the other it is a distinct disease.

**Etiology.**—The specific etiologic agent has not been isolated. It is probably contained in the buccal and nasal secretions, and transmission is accomplished chiefly, if not entirely, by direct contact. Transference of the infection through fomites or a third person is said to be possible, but its occurrence has not been proved. The danger of contagion is believed to be greatest during the eruptive period. Rubella, with rare exceptions, is an epidemic disease, and the majority of outbreaks occur in winter and spring. It is observed chiefly in children between the ages of 5 and 15 years, although adults who have not had the disease in childhood are frequently attacked. Infants under the age of six months apparently possess a certain degree of immunity. One attack almost invariably protects from others, but not from measles or scarlet fever.

**Symptoms.**—The *period of incubation* varies from 1 to 3 weeks. Prodromal symptoms are, as a rule, slight or altogether wanting. However, languor, headache, sneezing, cough, slight congestion of the conjunctivæ and enlargement of the cervical lymph-nodes are observed in some outbreaks. In the majority of cases the eruption appears within 24 or 36 hours, and frequently it is the first sign of the disease to attract attention. It appears first, as a rule, on the face and neck, and then spreads rapidly downward, the entire body being affected in the course of a day. It consists of more or less rounded, slightly elevated red spots, varying in size from a pin-head to a split-pea. The color of the lesions, while not distinctive is usually less dusky than that of the papules of measles, but not so bright as that of the rash of scarlatina. While the spots are in most cases fairly discrete, they sometimes coalesce, and occasionally the confluence is so pronounced that the exanthem appears as a diffuse erythema closely resembling that of scarlet fever (*rubella scarlatiniforme*). Even when the spots are closely placed they show little tendency to form the crescentic shaped blotches, which are so characteristic

of measles. The eruption rarely lasts more than 2 or 3 days, and sometimes it fades so rapidly that the face is almost clear by the time it is fully developed on the lower extremities. Slight furfuraceous desquamatiom usually, but not invariably, occurs upon the subsidence of the exanthem and continues for 2 or 3 days.

The general symptoms are scarcely ever pronounced and in many cases the patient feels perfectly well throughout the attack. The temperature usually rises as the rash appears, but it rarely exceeds 101° F., and the pyrexia seldom lasts longer than 2 or 3 days. The catarrhal manifestations are restricted, as a rule, to injection of the conjunctivæ, some soreness of the throat, occasional sneezing, and slight cough. Photophobia, lachrymation, and coryza are usually absent. Red macules sometimes appear on the fauces at the time of the exanthem, but Koplik's spots (bluish-white points surrounded by red areolæ) are not observed. The appearance of tongue is not peculiar as in scarlet fever.

The cervical and occipital lymph-nodes are enlarged in most cases and sometimes the swelling and tenderness are so pronounced as to cause considerable discomfort. This sign may also occur in measles and scarlet fever, but it is usually more conspicuous in rubella. As in measles, the blood commonly shows a hypoleucocytosis with a relative increase of the mononuclear cells.

*Complications* are rare. Bronchopneumonia, ileocolitis, otitis media, nephritis, stomatitis, and arthritis have been observed. *Relapse* occasionally occurs.

*Diagnosis.*—Measles and scarlet fever are the diseases with which rubella is most likely to be confused. The differential diagnosis from the former is considered on page 224 and from the latter on page 230. The *prognosis* is almost invariably good. The *prophylaxis and treatment* are similar to those of measles.

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## SMALLPOX

(Variola)

**Definition.**—Smallpox is an acute, specific, infectious and highly contagious disease, of from 2 to 3 weeks duration, characterized by an abrupt onset with chill, vomiting, headache and lumbar pain, an eruption which passes through the stages of papule, vesicle, pustule and crust, and fever which remits soon after the appearance of the eruption and again becomes high when the vesicles become pustules.

**History.**—Smallpox has probably existed since time immemorial, but no records of epidemics appear earlier than the sixth century. The term "variola" (from *varus*, a pimple) was first employed by Bishop Marius, of Lausanne, in describing an outbreak that occurred in Italy in 570 A.D. Rhazes, the Arabian physician, gave a clear description of the disease in the ninth century, but the credit of separating it from measles belongs to Sydenham (1624–1689). Smallpox was brought to North America by the Spaniards in the sixteenth century. Inoculation with the contents of variolous vesicles as a means of prophylaxis was introduced into England from Turkey by Lady Mary Wortley Montague in the eighteenth century. Where it was first practiced is unknown. In 1798 Edward Jenner published his memorable work on vaccination with cowpox virus as a protection against

smallpox. Previous to the discovery of Jenner smallpox was "the most terrible of all the ministers of death." It is estimated that the disease destroyed in Europe alone more than 200,000 lives annually.

**Etiology.**—Nearly everyone, unless protected by a previous attack or by vaccination, is susceptible to smallpox. Certain races, especially negroes, seem to suffer more severely than others. The disease occurs at all ages, even in fetal life, and is particularly fatal in young children. It may be introduced into a community from without at any season of the year, but epidemics occur chiefly in winter, probably because cold weather favors overcrowding and this gives more opportunity for the conveyance of the infection from person to person. Second attacks of the disease are very rare and almost invariably benign.

Smallpox is communicable from the first appearance of the symptoms until the complete separation of the scabs, but it is probably most contagious during the stages of suppuration and incrustation. The virus is known to be contained in the lesions of the skin and mucous membranes and in the blood. Whether it is also present in the physiologic secretions, when these are uncontaminated with discharges from the specific lesions, is doubtful.

Transmission is usually direct from the sick to the well, or mediate through clothing, bedding, etc., which have been in contact with the patient and which have been contaminated with his discharges. Conveyance through the clothing or effects of a well person is very uncommon. The question of the aërial convection of the virus is still debated, but the weight of evidence seems not to be in favor of it. It is possible that insects, especially flies, may sometimes aid in spreading the disease.

The infecting agent of smallpox has not been isolated with certainty. It is, however, one of the filterable viruses. Councilman,[1] Calkins[2] and others have regularly found in their cases the cell-inclusions, which Guarnieri[3] in 1892 described as protozoan parasites and named *Cytoryctes variolæ*, and believe them to be the cause of the disease. These bodies are found in the cells of the cutaneous lesions and occur in both the cytoplasm and nuclei. Bodies that are supposed to represent the first stage in the life cycle of the same organism are found also in the lesions of vaccinia, but they occur only in the cytoplasm of the epithelial cells, never in the nuclei. The conclusion of Councilman and his coworkers have not, however, been universally accepted. Ewing,[4] Proescher[5] and others claim that Guarnieri's bodies are not living parasites but products of cell degeneration.

Pyogenic organisms, especially streptococci, are always present in the ripe pustules and doubtless are the cause of the secondary fever and of the chief complications. Indeed, Councilman is of the opinion that bacterial infection is a more important factor in bringing about a fatal termination than the specific parasite.

**Morbid Anatomy.**—The specific lesion of variola is a focal degeneration of the stratified epithelium of the skin. Through the action of the specific toxin the cells of the upper strata of the Malpighian layer become edematous and undergo liquefaction, thus forming a cavity. In many of the cells, however, liquefaction is incomplete and the remaining protoplasm is transformed into a reticulum which divides the cavity into a number of compartments (*reticulating colliquation*). At the same time the cells of the lower strata

[1] Jour. Med. Research, 1903, vol. ix.
[2] Jour. Med. Research, 1904, vol. xi.
[3] Arch. per. Sci. Med., 1892, xxvi.
[4] Jour. Med. Research, 1904, vol. xii.
[5] New York Med. Jour., 1913, xcvii, 741.

swell up, lose their granular appearance, and become homogeneous (*ballooning colliquation*). These desquamative changes are accompanied by an exudation, at first serous, later more or less cellular and finally purulent. Edema, cellular infiltration, and hemorrhage in the corium often coexist with the lesions of the epidermis.

The characteristic central depression (umbilication) observed in many of the vesicles is due to the more rapid edematous swelling of the cells at the periphery of the pock than at the center and to the presence of an undissolved core of reticulum, which holds down the center of the roof of the pock, and not, as was formerly supposed, to the persistence of a hair follicle or sweat-duct.

Lesions similar to those occurring on the skin may also appear on the mucous membranes to which the air has free access, such as that of the nose, pharynx, esophagus, etc., but owing to the peculiar structure of mucous membranes the degenerated epithelial cells of the pock are soon cast off, and thus a shallow ulcer is formed instead of an umbilicated, multilocular vesicle. The liver is more or less enlarged, and microscopically exhibits the changes characteristic of cloudy swelling. The kidneys also show cloudy swelling, and occasionally evidences of acute glomerulonephritis. The spleen and the lymph-nodes generally are swollen. According to Councilman, Magrath and Brinckerhoff,[1] certain histologic changes occur in the bone-marrow, lymph-nodes and spleen so constantly and are so pronounced as to be almost characteristic. The most conspicuous of these changes is an infiltration, both diffuse and nodular, of mononuclear, basophilic wandering cells. The blood-forming tissue of the bone-marrow shows, in addition, many minute foci of necrosis surrounded by zones of wandering cells. Similar lesions also occur in the substance of the testicles and sometimes in the adrenals. The predominance of mononuclear, basophilic cells and the paucity of polymorphonuclear leucocytes in all the specific lesions is a striking peculiarity of the disease.

Non-specific inflammatory processes, the result of bacterial infection, such as bronchopneumonia, local abscesses, cellulitis, erysipelas, etc., are also present in many cases.

**Symptoms.**—The *period of incubation* is usually about 12 days, but it may be as long as 15 or even 20 days or as short as 8 or 9. The *invasion* is sudden and marked, as a rule, by chill, severe headache, pain in the lumbar region and vomiting. The vomiting may be accompanied by diarrhea, but in the majority of cases there is persistent constipation. The temperature rises rapidly and often reaches 103° or 104° F. on the evening of the first day. High temperature in adults is sometimes accompanied by delirium and in young children by convulsions. A prodromal rash of a morbilliform, scarlatiniform or hemorrhagic character not rarely appears on the second day or earlier and lasts 24 or 48 hours. The hemorrhagic rash, which is the most characteristic, commonly occupies the lower part of the abdomen and the upper part of the thighs, and consists of a close-aggregation of pinpoint sized petechiæ. It is usually, but by no means invariably, an indication of severe hemorrhagic variola. The duration of the initial stage is, as a rule from 2 to 3 days.

The *genuine eruption* of smallpox appears on the third day, in the form of small red macules, which are first visible on the forehead and wrists. In the course of 24 or 36 hours it invades successively the face, arms, trunk, legs and feet, although it always shows a decided preference for the exposed surfaces. The lesions rapidly develop into smooth round papules, which are

[1] Jour. Med. Research, 1904, xi.

peculiar in that they impart to the fingers a sense of hardness like small shot under the skin. After 2 or 3 days (5th or 6th of the disease) the papules become tense, shiny vesicles with red areolæ. The vesicles are quite uniform in size and many of them present a distinct depression in the center (umbilication). They are loculated, or divided into several compartments by a protoplasmic reticulum, so that when pricked with a needle at a single point they do not completely collapse. The vesicles gradually become opaque and by the sixth day of the eruption (ninth day of the disease) they are transformed into full round pustules, the umbilication disappearing in consequence of the erosion of the central core which formed it. Where the eruption is abundant, as on the face, the intervening skin is more or less diffusely swollen and injected, and in severe cases the patient's features may be so distorted as to be unrecognizable. Pain and discomfort are sometimes intense. A peculiar sickening odor emanates from the pus which is discharged from the lesions.

About the eighth or ninth day (eleventh or twelfth of the disease) *desiccation* begins. The contents of the pustules, many of which have ruptured, form yellowish-brown crusts, the subcutaneous edema subsides, and in about a week the crusts begin to fall off, although decrustation is usually not completed for a week or two more. The process of desiccation is frequently accompanied by severe itching. During this period a secondary rash, in the form of a mottled erythema, sometimes makes its appearance. It is probably of septic origin. After the separation of the scabs, the skin presents reddish-brown stains, which persist for several months. When the lesions affect the epidermis only, healing ensues without permanent disfigurement, but when they involve the true skin, cicatricial depressions or pits are left, which after the lapse of several months become whiter than the skin around them. Unfortunately, the most conspicuous pitting is on the face. At the end of severe attacks the hair may be lost and the nails shed.

The *mucous membranes*, especially those to which the air has free access, frequently share in the variolous process. The nose, mouth, and pharynx and even the esophagus, larynx and trachea may be extensively involved. The lesions are similar to those in the skin, except that superficial ulcerations take the place of the vesicles and pustules. Invasion of the nose manifests itself by occlusion of the nares and profuse discharge; of the throat, by soreness, salivation and dysphagia; of the larynx and trachea, by hoarseness, cough, and more or less dyspnea.

During the stage of invasion the *temperature* rises rapidly to 104° or 105° F. and occasionally to 106° F., often reaching its maximum on the second day. It continues high until the early period of the eruption when it falls several degrees, or in mild cases to normal. With the subsidence of the fever the distressing symptoms of the invasion abate, and the patient may seem to be convalescent. As soon, however, as the vesicles turn to pustules, or about the sixth day of the eruption or the ninth day of the disease, the temperature rises again, although not usually to its original height, and remains up with marked fluctuations for a week or ten days, or even longer, according to the extent of the eruption. This secondary fever is entirely due to infection with pyogenic organisms. During the pustular stage the constitutional disturbance is frequently that of the typhoid state, being marked by prostration, muscular twitchings, muttering delirium, a dry brown tongue, and involuntary evacuations. These symptoms rapidly disappear with the involution of the pocks and the formation of crusts.

Examination of the *blood* during the eruptive stage reveals in nearly all cases, except the mildest, a decided increase (10,000 to 20,000) in the number of leucocytes, chiefly of the mononuclear forms. In the absence of pyemic

complications, the percentage of polymorphonuclear leucocytes is almost always decreased, even when the pocks contain pus and streptococci.

The *urine* during the febrile period is scanty and high-colored and contains a diminished quantity of chlorids. In severe cases it is frequently more or less albuminous.

**Varieties.**—The following varieties are recognized: (1) Ordinary smallpox (Variola Vera), which, according to the number of pocks, may be (*a*) Discrete, or (*b*) Confluent; (2) Hemorrhagic smallpox; (3) Varioloid.

*Discrete smallpox* pursues the course already described. Although the symptoms are usually mild, their severity depends on the amount of the eruption. Not rarely the eruption is more or less confluent on the face, while it is discrete on other parts of the body.

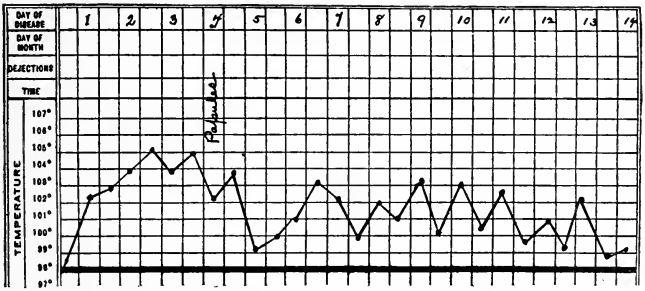


FIG. 10.—Temperature curve of a case of discrete smallpox in an adult, vaccinated once in infancy, showing initial fever, eruptive remission, and secondary or suppurative fever.

*Confluent smallpox* is a serious form of the disease. The invasion is stormy and the fever is intense. While the temperature declines during the papular stage of the eruption, the remission is usually slight and of short duration. Delirium which may be either of a maniacal or of a delusional character frequently develops at the commencement of the eruptive period. Even before the appearance of the papules, the patient's face may be markedly hyperemic and swollen. During pustulation the subcutaneous tissue throughout the body is usually infiltrated, the face, scalp, and hands, in particular, being bloated and the seat of intense pain and tenderness. The absence of this edema is of evil import. The mucous membranes suffer severely, so that salivation, dysphagia, hoarseness, and dyspnea are prominent symptoms. Septic complications, such as cellulitis, boils, abscesses, empyema, etc., are common. Prostration is profound, and to add to the patient's weakness and discomfort, diarrhea frequently supervenes. In fatal cases the pulse soon becomes very rapid and feeble, the typhoid state develops, the patient sinks into a comatose condition and death comes usually toward the end of the second week. If the patient recovers, it is only after a tedious convalescence and with great facial disfigurement.

*Hemorrhagic smallpox*, the most malignant form of the disease, is divided into *Variola Purpurica* and *Variola Pustulosa Hemorrhagica*, according as the hemorrhagic manifestations appear before or after the pocks.

Purpuric variola, or black smallpox, occurs most commonly in young

adults, and seems to show a special predilection for pregnant women. The characteristic feature of this type is the appearance of a diffuse purplish discoloration of the skin, with pectechiæ and ecchymoses, at the close of the initial stage. The face is swollen and the eyes are bloodshot. Bleeding also occurs from the various mucous membranes (hematemesis, metrorrhagia, epistaxis, etc.). The genuine exanthem is wanting or is slight and imperfectly developed. There may be delirium or stupor, but in many cases the mind is clear until the end. Death is invariable and occurs, as a rule, on the fourth or fifth day.

In hemorrhagic pustular variola the eruption always develops to a greater or less degree, but at a certain stage—papular, vesicular, or pustular—the pocks become infiltrated with blood. Petechiæ may be observed also in regions free from the pocks and bleeding may occur, as in purpuric variola, into the conjunctivæ and from the nose, mouth, rectum, uterus, etc. The temperature is rarely high, but the adynamia is intense, and recovery is very rare.

The term *modified smallpox, or varioloid*, is applied to a type of the disease in which the course of the eruption is shortened and the secondary fever is very slight or wanting. This mitigation of the symptoms usually is the result of a certain degree of protection secured by vaccination, or, more rarely, by an antecedent attack of smallpox; but occasionally it is to be attributed to a natural insusceptibility. The initial symptoms occur as in ordinary variola, but, as a rule, they are mild. The eruption is usually scanty and discrete, but occasionally it is quite extensive. The pocks, which are likely to be small and superficial, mature more rapidly than those of unmodified smallpox, and frequently desiccate in the vesicular stage. If pustules form, they dry up on the sixth or seventh day, forming thin crusts which soon drop off. The fever may be high at the onset, but it abates abruptly on the appearance of the eruption and rarely rises again unless there are complications. Owing to the superficial character of the lesions there is little or no scarring.

The disease known as *alastrim*, occurring in South America and the West Indies, is probably a mild form of smallpox, similar to varioloid, although the initial fever is pronounced and the pocks are often very numerous.

The term *variola sine eruptione* has been applied to an extremely benign form of varioloid in which convalescence begins with the close of the initial stage, no eruption appearing.

**Complications.**—*Boils, impetigo, abscesses, erysipelas*, and even *gangrene* not infrequently result from secondary infection of the skin. Ocular complications are less common since the introduction of vaccination, but *severe conjunctivitis* and *ulceration of the cornea* sometimes supervene when the lids are involved in the pustulation. Pocks rarely form upon the eye-ball. The presence of pustules in the throat and upper air-passages occasionally leads to *otitis media, edema of the larynx* or *bronchopneumonia. Pleurisy*, especially empyema, is not very uncommon, but *endocarditis* and *pericarditis* are rare. *Myocarditis* is more frequent. Albumin and casts are often found in the urine, but genuine *nephritis* is an exceptional complication. *Orchitis* has been observed. *Arthritis* sometimes is met with, especially in children. Areas of softening and blood extravasation occasionally occur in the brain producing *aphasia, monoplegia* or *hemiplegia*, or in the spinal cord, producing *paraplegia. Insanity* and *epilepsy* have been noted. *Delirium tremens* is frequently seen in persons addicted to alcohol. In 1892 Combemale[1] collected 10 cases of smallpox in which *peripheral neuritis* devel-

[1] Archiv. gén. de méd., June, 1892.

oped. The *alopecia*, which is frequently observed after severe cases, is not likely to be permanent.

**Diagnosis.**—The recognition of smallpox is sometimes difficult, especially when the eruption is just appearing or is modified by vaccination. The disease may be mistaken for varicella, pustular syphiloderm, measles, certain drug rashes, and impetigo contagiosa.

*Varicella.*—In varicella prodromal symptoms are usually absent and the constitutional disturbance is slight. The eruption appears on the first day; it comes out in successive crops, and therefore lesions in various stages of development are often seen side by side, even within small areas; and, especially important, it shows a decided predilection for the covered surfaces, being scanty on the distal parts of the extremities, and rarely found on the palms of the hands or the soles of the feet. It may be maculo-papular at first, but it becomes vesicular within a few hours. The vesicles are superficial, usually unilocular, soft to the touch and easily ruptured. They vary considerably in size, are often oval rather than round, and are not umbilicated. Desiccation begins in two or three days, the vesicles becoming irregularly puckered at the periphery, and presenting a depressed blackish crust in the center—a highly characteristic appearance. Finally, in doubtful cases in children the presence of a typical vaccinal cicatrix is strong presumptive evidence against variola.

*Pustular Syphiloderm.*—In syphilis a history of venereal infection is usually obtainable; there are often other evidences of the disease, such as mucous patches, alopecia, etc.; the onset is gradual; the constitutional disturbance is mild; and the fever, which is, as a rule, moderate and very irregular, does not remit on the appearance of the exanthem. The eruption comes out in crops, is of patchy distribution, frequently affects the trunk more than the face, and pursues a relatively chronic course. The pustules are not round and full as in smallpox, but are conical and mounted on papular bases.

*Measles.*—In this disease vomiting and lumbar pains are usually absent, the initial symptoms being comparatively mild; catarrh of the conjunctivæ and respiratory tract is a prominent feature; the fever does not remit on or shortly after the appearance of the exanthem; the buccal spots described by Koplik are rarely wanting; hypoleucocytosis is the rule; and the papules are commonly larger, more irregular in outline, and less elevated than those of variola, and, instead of being "shotty" to the touch, have a soft velvety feel.

*Drug rashes*, especially those produced by bromids, iodids or copaiba, may simulate the eruption of smallpox, but the history and the absence of constitutional symptoms will usually suffice to prevent an error in diagnosis.

*Impetigo Contagiosa.*—The lesions of impetigo are usually confined to the face and hands, are primarily vesiculopustular or bullous, are accompanied by little or no constitutional disturbance, and rapidly dry into thin, yellowish, wafer-like crusts.

*Generalized vaccinia* is not likely to be mistaken for smallpox as it accompanies a typical vaccine lesion and is not preceded by high fever, headache, vomiting, etc.

**Prognosis.**—The prognosis depends on the virulence of the epidemic, the age and vaccinal state of the patient, and the type of the attack. The mortality varies considerably, both in the vaccinated and unvaccinated, in different epidemics. In children under 5 years of age and in old persons unmodified smallpox is very fatal. Among persons having one or two good vaccine scars the death-rate is low, ranging from 1 or 2 per cent. to 7 or

8 per cent., according to the epidemic. In 2335 cases occurring in vaccinated persons (good scars), and observed by Welch[1] in the Municipal Hospital, Philadelphia, the mortality was 6.5 per cent., while in 3687 unvaccinated persons it was 41.82 per cent. The average death-rate in the unvaccinated is apparently not less than 30 per cent. In the discrete form of smallpox the prognosis is usually favorable, in the confluent form very grave, and in the hemorrhagic form almost hopeless. In individual cases, unfavorable signs are hyperpyrexia, protracted delirium, an erythematopurpuric prodromal rash, and a sudden subsidence of the facial swelling with flattening and shrinking of the pustules.

Variola is particulary fatal in pregnant women, and abortion or premature birth is the rule.

**Prophylaxis.**—The preventive measures against smallpox include the immediate isolation of the patient (preferably in a special hospital); the disinfection of all objects that have been in contact with him; the vaccination of everyone who has been or is likely to be exposed to the contagion; the segregation of all exposed persons for 3 weeks from the date of the last exposure, or until protected by vaccination; and the thorough disinfection and cleansing of the premises in which smallpox cases have developed or have been treated.

**Treatment.**—Absolute rest in bed, light bed-clothing, an easily assimilable diet, and the free use of water are requisites of treatment. The sick-room should be well ventilated, screened, and kept at a temperature of 65°–68° F. In the invasive stage, milk and light broths are suitable forms of nourishment. Orangeade, lemonade, etc., are usually well received, and, in addition to supplying an abundance of water, increase slightly the caloric value of the diet. During the stage of suppuration, the most exhausting period of the disease, the diet should be as nutritious as the patient can tolerate. Unfortunately, the soreness of the throat and mouth often makes the ingestion of sufficient nourishment difficult. As a rule, however, eggs, cream, well-cooked farinaceous foods, and gelatin preparations can be introduced in addition to milk. When there are symptoms indicative of exhaustion, alcohol in the form of brandy or whiskey, may often be used with advantage. It adds calories to the diet, stimulates digestion, and promotes sleep. Quinin, in small doses, is also of service in the adynamia of sepsis. Stimulants (digitalis, caffein, strychnin, camphor) are called for in the event of *circulatory failure.*

The severe *lumbar pains* will require the application of hot-water bags and the administration of morphin hypodermically, or of acetphenetidin in moderate doses by the mouth. Sinapisms should not be used, as the pocks always appear in great profusion upon irritated surfaces. *Gastric irritability* may usually be controlled by the use of cracked ice, champagne, bismuth subcarbonate, cerium oxalate or cocain. *Restlessness, jactitation,* and *insomnia* will require the use of morphin, bromids or chloral. Patients who are actively delirious or who are the subjects of delusions must be carefully watched and, if necessary, strapped in bed with folded sheets, since they not rarely attempt to escape through the window or even to commit acts of violence. The fever of the initial stage is best controlled by sponging the body with cold water and applying an ice-bag to the head. The fever of the suppurative stage may be kept within bounds by cool or tepid packs. Cold baths are not, as a rule, well borne. An attempt should be made to keep the *nasopharynx* clean. For this purpose Dobell's solution, diluted with 2 or 3 parts of water, or boric acid solution (2 per cent.) may be used as an

[1] Welch and Schamberg, Acute Contagious Diseases, 1905, 280.

irrigation or spray or applied by gentle swabbings. If the secretions are very offensive a solution of potassium permanganate (1:4000) may be substituted.

*The eyes* should also be kept clean by frequent applications of warm boric acid solution—10 grains to the ounce (0.65 gm. to 30.0 mils.) In purulent conjunctivitis a few drops of argyrol (10 to 20 per cent.) may be dropped into the conjunctival sac once or twice a day. If keratitis supervenes atropin should also be used to allay inflammation, produce mydriasis and prevent iritis, and the eyes protected with cold or warm compresses. *Dysphagia* is often benefited by pellets of ice, demulcent drinks, sprays of cocain (2 per cent.) or lozenges of orthoform (1 gr.–0.06 gm.).

When *laryngeal symptoms* are threatening the use of the steam tent and of inhalations of medicated steam (compound tincture of benzoin, eucalyptol, etc.) are often of great benefit. If edema of the larynx supervenes it may be necessary to scarify the affected tissue or to perform tracheotomy.

*The Eruption.*—The application of cold compresses is, perhaps, the best means of allaying burning and itching. Compresses wet with a cold solution of boric acid (3 per cent.) may be kept constantly on the face, hands and forearms. Ointments containing phenol (3 per cent.) are also effective. Many remedies have been recommended to prevent pitting, but it is doubtful whether any are really efficacious. An old plan was to open the vesicles and touch their bases lightly with a stick of silver nitrate. Dujardin-Beaumetz recommended very highly an ointment of sodium salicylate (4 parts) and cold cream (100 parts). Hebra found continuous warm baths of value. Schamberg claims good results from applications to the face, once or twice a day, of tincture of iodin, undiluted, or, if the skin is especially sensitive, diluted one-half. Finsen, Feilberg and others have advocated the exclusion of the chemical rays of light from the sick-room, red light only being admitted, but this plan of treatment has not been found particularly efficacious by those who have adopted it, and has the drawback of putting a check on the supply of fresh air. In the stage of desiccation warm alkaline baths followed by inunctions with cold cream or olive oil are useful in allaying itching and in hastening the removal of the crusts.

Quarantine should be continued until decrustation is completed. After all the crusts are detached the patient should be given a bath of corrosive sublimate solution (1:10,000) and then a soap-and-water bath and a thorough shampoo. Finally, he should be removed to another room and given entirely clean underclothing.

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## VACCINIA

### (Cowpox)

**Definition.**—Vaccinia is an acute specific disease acquired by inoculation with the virus of cowpox, characterized by the development of a pock similar to those of variola at the site of inoculation and by slight febrile disturbance, and exercising a protective influence against variola of several years' duration.

**History.**—The value of vaccination as a means of conferring immunity against smallpox was first established on a firm basis by Edward Jenner, who was led to his immortal discovery by the belief long entertained by the dairymaids of Gloucestershire that individuals who had contracted peculiar sores

upon their hands by contact with like sores on the udders of cows were never attacked with smallpox. On May 14, 1796, he inoculated James Phipps, a lad of eight years, with virus obtained from vesicles on the hand of Sarah Nelms, a milkmaid. The vaccination proved successful and a subsequent inoculation of the boy with smallpox matter on the second of the following July was without result. Jenner continued his observations and at the end of two years announced his results to the world. The operation was first performed in America on July 8, 1800 by Dr. Benjamin Waterhouse, the first Professor of Physic at Harvard University, who labored so zealously to extend the incalculable benefits of the new discovery that he became known as the "Jenner of America."

Prior to the discovery of vaccination, smallpox had been robbed of some of its terrors by the practice of *inoculation*, introduced into Europe by Lady Mary Wortley Montague, who as the wife of the British Ambassador to Turkey had been impressed with the efficacy of the procedure in Constantinople, whither it had been imported from Persia and China. In this procedure smallpox was imparted intentionally by the injection of matter from a variolous pock into the skin. The disease thus produced, while much milder than when acquired in the natural way, was scarcely less effectual in protecting against a second attack. Inoculated smallpox, however, occasionally proved fatal; moreover it was contagious, and therefore served to keep the disease prevalent in the community. For these reasons the practice was discontinued soon after the discovery of vaccination, and in 1840 it was declared illegal both in England and France.

**The Disease in Cattle.**—The view originally advanced by Jenner that cowpox is smallpox modified by passage through the comparatively insusceptible tissues of the cow is generally, although not universally, accepted. The disease formerly appeared spontaneously in dairies at long intervals, attacking primarily young milk-cows. It was characterized by an eruption which was confined to the udders and passed through the various stages of the variolous pock. The vesicles were usually broken in the act of milking, and thus the infection was rapidly disseminated through the entire herd. At present vaccinia is produced artificially in cows by inoculating them with virus obtained from vaccine vesicles in human beings. Attempts to produce vaccinia in the cow by inoculating the animal with smallpox matter have frequently failed, but the efforts of a number of experimenters, including those of Thiele, Ceeley, Badcock, Copeman, and more recently of Voigt and Haccius, have been entirely successful. In several instances the affection thus artificially produced in the cow has been transmitted to thousands of human beings, with all the phenomena and effects of cowpox, and has then been successfully reinoculated in the cow.

A disease bearing a close relationship to vaccinia and variola occurs in a number of the lower animals besides the cow, notably in the horse and sheep. Horsepox is very similar in its nature to cowpox, while sheeppox resembles human smallpox in producing a generalized eruption and in being communicable by intimate association from one sheep to another. No instance has been reported, however, in which man has contracted pox from the sheep or the sheep has contracted the disease from man.

**Etiology.**—L. Pfeiffer, Guarnieri, Wasielewski, Councilman and others have described in the lesions of smallpox and cowpox certain spherical bodies, which they regard as protozoa and which they believe to be the cause of the variolous diseases. These organisms, designated by Guarnieri the "cytoryctes variolæ" and "cytoryctes vaccinæ" respectively, appear to undergo a double cycle of development in the human host. They appear

first in the cytoplasm of the epithelial cells and there break up into spores. These subsequently enter the nuclei of the cells where they undergo a second segmentation. According to Magrath and Brinckerhoff,[1] when the monkey is inoculated with the virus of smallpox skin lesions are produced in which the entire developmental cycle of the parasite can be followed through both the cytoplasmic and intranuclear stages. Councilman and his coworkers believe that in vaccinia the parasite does not develop beyond the extranuclear stage, as intranuclear forms have never been seen in this disease. The parasitic nature of Guarnieri's bodies has not been universally accepted. Ewing,[2] Proescher,[3] Paschen,[4] and others claim that these bodies are only the end products of cell degeneration.

**Periods at which Vaccination should be Performed.**—Ordinarily, unless contraindicated by certain conditions of ill health, vaccination should be done during the first year of life, preferably at the fourth or fifth month. When smallpox is prevalent, however, it should not be deferred more than 24 or 48 hours after birth. Except in the course of a variolous epidemic, vaccination should be delayed if the child is suffering from acute gastro-intestinal disturbance, eczema, any suppurative skin disease, or tuberculous adenitis.

Insusceptibility to primary vaccination is rare, and usually, but not invariably, indicates immunity to smallpox, at least for the time being. When vaccination proves unsuccessful it should be repeated at intervals a number of times, and preferably with different strains of virus. It frequently happens that a person who is immune to vaccinia at one period is susceptible at another. As in many cases the protection against variola afforded by a successful vaccination in infancy is not permanent, but gradually diminishes with lapse of years and finally becomes extinct, the operation should be repeated at least twice—at the seventh year and again at puberty. As an extra precaution all persons, even those with 3 good vaccinal scars should be vaccinated when smallpox breaks out in a community.

Pregnancy should not be regarded as a contraindication. The average period of immunity conferred by vaccination is believed to be about 7 years. Revaccination is not rarely successful, however, after intervals of 2 or 3 years, but undoubtedly immunity from smallpox, following vaccination, lasts longer than immunity from reinfection with vaccine virus.

**The Virus.**—At the present time cowpox virus is universally employed for producing vaccinia in human beings. Formerly, material taken from the pustule or scab of a person previously vaccinated was also used, but owing to the risk of transmitting syphilis and other diseases this source has been entirely abandoned. Cowpox virus may be dried on pointed strips of celluloid ("dry points"), but it is preferably mixed with glycerin and preserved in sealed capillary tubes. The admixture of glycerin with the virus serves to preserve it and to free it from aërobic bacteria, especially pus cocci. Properly perserved in sealed tubes, "glycerinated virus" retains its full activity, under favorable conditions, for at least three months.

**Technic of Vaccination.**—The inoculation is usually made on the outer aspect of the arm over the insertion of the deltoid muscle, but in female infants, for esthetic reasons, it may be made on the leg over the head of the fibula. The part selected should be thoroughly cleansed, first with soap and water, then with alcohol, and finally with pure water. Many methods

[1] Jour. of Med. Research, Feb., 1904
[2] Jour. Med. Research, 1904, xii.
[3] New York Medical Jour., 1913, xcvii.
[4] Münch. med. Woch., 1906, liii.

of performing the operation are recommended. The simplest is to make with a sterile needle a number of cross scratches, only deep enough to allow of a little oozing of pinkish serum. The withdrawal of blood is to be carefully avoided, as it tends to wash away the vaccine material. The virus is now applied and well rubbed into the exposed lymphatic spaces by additional scarification. A shield may be worn for a few hours, until the wound has become perfectly dry; after that it should be discarded, since it serves, especially if tight fitting, to intensify the inflammatory reaction. It is desirable, however, to protect the vesicle from injury and secondary infection by a few folds of clean linen or a sterile gauze compress.

Goodall[1] advocates vaccination by subcutaneous injection, claiming that it is less painful than scarification and virtually eliminates the danger of secondary infection.

**Symptoms of Vaccinia.**—Slight redness usually occurs almost at once after the operation, but subsides, as a rule, within 24 hours. On the third or fourth day a papular elevation appears at the site of inoculation. By the sixth or seventh day the papule becomes a distinct vesicle filled with clear serum. The vesicle gradually enlarges and by the eighth or ninth day reaches its full size. It is then of a pearly color, depressed in the center (umbilicated) and surrounded by a red areola of greater or less extent. Usually at this period there is a feeling of tension and heat, with considerable itching. About the eleventh day the inflammation begins to subside, the areola grows paler, the vesicle becomes opaque, and desiccation appears at its center. By the fifteenth day the pock is completely transformed into a yellowish or reddish-brown crust, which is gradually detached and falls off during the third or fourth week, leaving behind a dusky red scar. In the course of two or three months the scar becomes white. A typical vaccine cicatrix is round or oval, sharply circumscribed, depressed, and with minute pits or foveolæ in its base.

The evolution of the pock is usually accompanied by a certain degree of constitutional disturbance, consisting of chilliness, slight fever, anorexia, restlessness and malaise. Leucocytosis may also be present.

**Variations.**—Certain variations in the course of vaccinia may occur without impairing its protective power against variola. Thus, the process may be somewhat retarded, although otherwise normal, a week or more elapsing before the development of the vesicle. Less frequently the process is accelerated, even in primary vaccinations, and the pock attains its full development as early as the seventh day. In some instances a number of small supernumerary vesicles develop in the red area around the site of inoculation, and rarely pocks appear spontaneously in successive crops on various parts of the body (*generalized vaccinia*).

**Spurious Vaccination.**—Sometimes the eruption is entirely irregular and in such event the vaccination should be regarded as unsuccessful. Somewhat frequently the pock develops slowly and does not advance to the vesicular stage, but remains a hard red papule (raspberry excrescence) for several weeks and finally disappears without leaving a cicatrix. In another spurious form the vesicle is conical and filled with puriform fluid almost from the beginning, and an irregular areola forms as early as the fourth or fifth day.

**Revaccination.**—The results of revaccination vary with the vaccinal susceptibility still retained by the patient. If antibodies against vaccine virus are present in the blood, an areola, with or without a papule, may appear at the end of 24 hours and subside in 72 hours (*reaction of immunity*), or a red areola may form in 24 hours and develop into a small vesicle, which

[1] Lancet, 1919, No. 5007, 285.

matures on the fifth or sixth day and then very rapidly subsides (*vaccinoid*). On the other hand, if the individual's insusceptibility has completely lapsed revaccination may produce a typical vaccine pock.

**Complications.**—Complications are rare and for the most part preventable. At the present day they can usually be traced to a lack of aseptic precautions at the time of the operation or to inadequate protection of the lesion against extraneous organisms. *Local inflammatory affections* are the most common and include cellulitis, lymphangitis, inflammation of the regional lymph-nodes, erysipelas, deep ulceration, and gangrene. *Certain skin diseases*, especially urticaria, generalized erythema (erythema vaccinicum), erythema multiforme, and impetigo contagiosa exceptionally follow in the wake of vaccination. In some instances, at least, their occurrence is purely coincidental. Eczema may be called forth or aggravated by the operation, but the danger is slight. Indeed, Duhring, Tait, Stelwagon and others attest the occasionally curative influence of vaccinia in this disease. Children sometimes convey the infection from the first site of inoculation to different parts of the body by scratching themselves. Secondary pocks have been observed in the nose, eye, mouth, and elsewhere. *Tetanus* is the most serious complication of vaccinia. It is due in the vast majority of cases to infection of the wound at some period subsequent to the insertion of the virus and rarely to infection through the virus itself.

**Value of Vaccination.**—That vaccination always protects against smallpox for a time, generally for many years and sometimes for life, is attested by incontrovertible evidence. From one of the commonest and most terrible of plagues it has become in civilized communities one of the rarest of the acute infections. In London during the period between 1771 and 1800 the number of deaths from smallpox was 57,267, whereas in the period between 1801 and 1830 it was 27,382. At the present time the average annual death-rate for the whole of England is not over 600 or 700.

The value of compulsory vaccination and revaccination is well shown in the marked difference between the death-rate from smallpox in Germany and Austria. In Germany, where vaccination and revaccination have been universally practiced, the average yearly mortality from smallpox per million of population between 1893 and 1897 was only 1.1, and in Austria, where the vaccination requirements have been very lax, the average death-rate for the same period was 99.1.

When properly vaccinated, persons employed in smallpox hospitals are rarely attacked by the disease. Welch states that inthe Municipal Hospital of Philadelphia, during a period of 34 years, in which time over 9000 cases of smallpox were treated, not a physician, nurse or attendant, who had been successfully vaccinated or revaccinated prior to going on duty, contracted the disease.

Before Jenner's time smallpox was to a great extent a disease of childhood, but at the present day the vast majority of the cases occur at later and less protected ages. It has been estimated that children under 5 years, including the unvaccinated, now supply only 3.07 per cent. of the deaths from smallpox and adults from 20 to 60 years of age, 77 per cent.

When smallpox does occur in the vaccinated it is much less fatal than when it attacks the unvaccinated. In Gayton's 10,403 cases treated in Homerton Hospital between 1873–1884, the death-rate among the vaccinated 8,234, was 10.5 and among the well vaccinated only 3 per cent.; whereas among the unvaccinated 2,169, the death-rate was 43.4 per cent.

If practiced within 3 or 4 days after exposure to smallpox infection vaccination may stay the disease or at least modify its course. Nothing is

gained, however, by vaccinating patients who are already in the initial stage of the disease. Hibbert (Lancet, May 20, 1905) attempted vaccination in 20 cases of smallpox after the appearance of the eruption and produced a characteristic vesicle in 11 instances.

## CHICKENPOX

(Varicella)

**Definition.**—Chickenpox is an acute, specific, infectious and contagious disease, of benign nature and short duration, characterized by slight fever and a discrete vesicular eruption appearing in successive crops.

The disease was first differentiated from smallpox by Fuller in 1730.

**Etiology.**—Chickenpox is endemic in most populous communities and from time to time becomes epidemic. It occurs chiefly in young children, most commonly between the ages of 1 and 6 years. Adults, however, are occasionally attacked. It is usually transmitted by direct contact, but mediate infection through fomites or a third person seems to be possible.

The disease is communicable probably from the latter part of the period of incubation until the disappearance of the scabs. Second attacks are rare. The inciting agent is unknown. Some investigators have found inclusion bodies in the epithelial cells of the vesicles which they believe to be analogous to cytoryctes variolæ (see p. 234). Whatever its nature, the virus is apparently filterable. Chickenpox bears no relation to smallpox and one disease does not protect against the other.

**Symptoms.**—The *period of incubation* is usually about 2 weeks. The invasion may be marked by chilliness, general aching, anorexia and malaise, but, as a rule, the *eruption* is the first indication of illness. Rose-red papules appear first on the back and face and then spread to the chest, abdomen and limbs. In contrast with smallpox, the trunk is especially involved, the face, arms, and legs being only lightly affected, and the palms of the hands and the soles of the feet usually escaping entirely. In the course of a few hours the papules become distinct vesicles of crystal transparency. The transition is effected so quickly that the papular stage is often overlooked. The vesicles are superficial, round or oval, commonly surrounded by a red areola and very delicate, so that they are easily ruptured. They are almost always discrete and the intervening skin is neither hyperemic nor swollen. The pocks vary considerably in size, some being no larger than a pin-head while others reach the dimensions of a large pea. The umbilication so characteristic of variolous pocks is rarely observed. After 24 or 48 hours the unbroken vesicles are changed into pustules and then desiccation begins, each pock soon becoming irregularly puckered at the periphery and presenting a depressed brownish or blackish crust in the center. The crusts usually separate in the course of a few days or a week, leaving temporary red stains. Not infrequently a few pocks invade the papillary layer of the true skin and produce permanent scars.

The eruption does not come out all at once, but in successive crops over a period of three or four days, hence pocks in various stages of development may often be seen at the same time within a comparatively small area—a highly characteristic feature. The total number of lesions is not rarely less than a score, but it sometimes reaches several hundred. Occasionally there is considerable itching. In some instances pocks also appear on the mucous

surfaces to which the air has free access, especially those of the mouth pharynx and larynx.

As a rule, a slight *febrile disturbance* accompanies the eruption, but the temperature does not usually rise above 100° or 101° F. In exceptional cases, however, the temperature may rise to 104° F. or even higher. The blood picture is variable. The number of leucocytes may be normal, somewhat decreased or slightly increased. The superficial lymph-nodes are sometimes enlarged. The entire *duration of the disease* does not usually exceed a week or ten days, but exceptionally some of the crusts adhere for two or three weeks or longer.

**Variations.**—Atypical cases are uncommon. Occasionally, as a result of accidental secondary infection, certain of the vesicles enlarge, suppurate, and become surrounded by a zone of gangrene (*varicella gangrenosa*); in rare instances hemorrhages occur into the vesicles and also from the mucous membranes (*varicella hemorrhagica*); and in other cases the vesicles become very large, forming bullæ and resembling pemphigus (*varicella bullosa*).

**Complications.**—Complications are rare. *Impetigo*, *erysipelas*, and even *septico-pyemia* may result from secondary infections of the pocks. *Acute nephritis* is probably the most common complication. According to Cerf[1] 40 cases had been reported up to 1900.

*Multiple arthritis* has been described by several writers. Marfan and Halle have recorded two instances of *varicellous laryngitis*, in one of which life was saved by recourse to tracheotomy. Henoch and E. Oppenheimer speak of *varicellous conjunctivitis*. Chickenpox is occasionally associated with other infections, especially measles, scarlet fever and diphtheria.

**Diagnosis.**—Chickenpox may be confused with smallpox and with impetigo contagiosa. Differentiation from *smallpox* is considered on p. 239. In *impetigo contagiosa* the lesions are less disseminated, have a predilection for the face and hands, are usually larger and show a marked tendency to coalesce and form irregular patches.

**Prognosis.**—This is almost invariably good. A fatal issue is exceptional and when it occurs it is due usually to a complication and only rarely to the toxemia of the disease.

**Prophylaxis and Treatment.**—As chickenpox is usually so benign in its effects, strict measures of control are usually regarded as unnecessary. It is advisable, however, to isolate the patient until the crusts have fallen off and to keep contacts from other susceptibles, especially delicate children, for a period of 21 days. After the patient has recovered the sick room should be thoroughly cleaned and well aired. Kling[2] speaks favorably of inoculation as a prophylactic measure. He uses material from the vesicles of children with varicella and inserts it into the skin as in vaccination against smallpox. He asserts that the eruption rarely develops outside of the area of insertion and that none of the inoculated children acquired varicella, while of 108 who were not inoculated, 73 per cent. were attacked. Hess and Unger[3] were not successful with Kling's method of vaccination, but found it possible to bring about immunity by means of intravenous injections of the contents of the vesicles. The injections did not cause either local or systemic reaction.

Special *treatment* is rarely required. The patient should be confined to bed and given a light diet while the fever lasts. Scratching should be prevented, since it increases the liability to secondary infection of the pocks and to permanent scarring. Itching may be allayed by dusting the affected

[1] Arch. de Med. des Enf., Feb., 1901.
[2] Amer. Jour. Dis. of Child., 1918, xvi, 34.
[3] Berlin. klin. Woch., 1913, l, 2083; ibid., 1915, liii, 13.

areas freely with a powder of boric acid and zinc oxid (1 part of the former to 2 parts of the latter) or smearing them lightly with carbolized oil.

## ACUTE RHEUMATISM

(Rheumatic Fever)

**Definition.**—Acute rheumatism is an infectious but non-contagious disease, characterized by an irregular fever, polyarthritis, and in many cases inflammation of the cardiac tissues, especially the endocardium.

**Etiology.**—While it is not disputed at the present time that acute rheumatism is an infectious disease, much confusion exists as to the nature of the *infecting microörganism*. Considerable evidence has accumulated in favor of the view that a streptococcus is the inciting agent. In 1894 Leyden[1] found in the endocardial lesions of several cases of acute rheumatism a small streptococcus or diplococcus, probably identical with that described by Popoff[2] in 1887. Four years later Triboulet and Apert[3] isolated from the blood of a patient with rheumatic fever a similar organism, which in rabbits caused non-suppurative arthritis, endocarditis and pericarditis. Later, these observations were confirmed by Wassermann and Menzer[4] in Germany by Poynton and Paine,[5] Beaton and Walker,[6] Beattie[7] and Coombs, Miller and Kettle[8] in England, and by Lewis and Longcope,[9] Rosenow[10] and others in America. While the majority of investigators are in agreement as to the identity of these organisms, the question of their specificity has been seriously disputed. The resemblance, both morphologic and cultural, between the streptococci isolated from the blood and joints of patients with acute rheumatism and streptococci from other sources is very close; moreover, a number of investigators have been able to produce non-destructive arthritis and endocarditis in rabbits by inoculating these animals intravenously with streptococci from diverse sources. Hence, the view held by some observers, among others Menzer, that acute rheumatism is not a disease *sui generis*, but a manifestation of a more or less attentuated streptococcic septicemia has considerable evidence in its favor. Certainly the whole subject needs further elucidation before it can be accepted as an established fact that the exciting cause of rheumatism is a specific coccus—the *Diplococcus rheumaticus* of Poynton and Paine. Rosenow's conclusions in this connection are novel and interesting. He believes that a transmutation of streptococci can occur within the body tissues and that acute rheumatism is caused by certain strains of comparatively low virulence which have emanated from some local focus of infection where they have acquired an elective affinity for the joints. Possibly, as the experimental studies of Faber[11] suggest, the attack of rheumatism is not precipitated until the joints have undergone a certain

[1] Deutsch. med. Woch., 1894.
[2] Quoted by Dunn, Jour. Amer. Med. Assoc., 1907, xlviii.
[3] Compt. rend. de la Soc. de Biol., 1898, No. v, Gaz. des Hôp. des Paris, t. lxxv.
[4] Berlin. klin. Woch., 1899, No. 29.
Aet. des akuten Gelenkrheumatismus, Berlin, 1902.
[5] Lancet, 1900, vol. ii.
[6] Brit. Med. Jour., 1903, vol. i.
[7] Brit. Med. Jour., 1904, vol. ix.
[8] Lancet, 1912, vol. ii.
[9] Amer. Jour. Med. Sci., 1904, vol. cxxviii.
[10] Jour. Amer. Med. Assoc., 1913, vol. lx.
[11] Jour. Exp. Med., 1915, xxii.

degree of sensitization as a result of the persistent adsorption of streptococci. Owing to the frequency of tonsillitis in the early stages of the disease, it is probable that the tonsil is an important portal of entry for the organism, whatever its nature.

Acute rheumatism is a common disease. In the large municipal hospitals of Europe and America it constitutes from 3 to 7 per cent. of the total admissions. Although widely distributed, it prevails more extensively in *temperate regions* than elsewhere and is especially favored by *damp* and *changeable weather*. In this country the maximum number of cases is usually observed during the *spring months*, while in England the highest incidence of the disease occurs in the *autumn*. But in all countries the prevalence and severity of rheumatism are subject to decided variations, which can be attributed more readily to *epidemic influence* than to special meteorologic conditions.

Acute rheumatism is observed most frequently in *youth* and *early adult life*, although children over five years of age are often attacked. It is rare in infancy. *Sex* does not seem to exert any special influence upon the frequency of the disease. *Occupations* that entail exposure to the vicissitudes of weather are attended with a notable liability to acute rheumatism; hence the disease is common among laborers, drivers, plumbers, and domestic servants. *Heredity* is a factor of some importance, although it probably exerts less influence than is commonly supposed. As to the close association of rheumatic fever in many instances with a *single severe exposure* to *cold and wet* there can be no question. As in the case of pneumonia, chilling probably acts by lessening the resistance of the tissues to infection. Occasionally, *traumatism*, by creating a *locus minoris resistentiæ* determines the localization of the disease.

No other infection recurs in the same individual with such frequency. In some series of cases the percentage of recurrences has been over 40.

**Morbid Anatomy.**—The affected joints are the seat of an acute exudative inflammation, which is not essentially different from that resulting from mild forms of traumatism. The joint cavity is distended with yellowish turbid serum, mixed in some cases with fibrinous flocculi. The ligaments, the capsule, and the synovial membrane, especially, are injected and slightly swollen. In severe cases the cartilages may be eroded in places and the periarticular tissues infiltrated with the products of inflammation. The process is somewhat peculiar, however, in that it rarely, if ever, ends either in suppuration or in permanent injury to the joint.

In addition to the arthritis, inflammatory lesions in the heart are also present in a very large proportion of cases. While endocarditis is usually the most pronounced cardiac lesion, myocarditis is seldom absent, and in many instances pericarditis is also observed. The endocarditis involves most frequently the mitral valve, although the aortic and tricuspid valves are not rarely affected. It is usually of the simple or benign type (see p. 669). The myocarditis is peculiar pathologically in presenting the so-called submiliary nodules of Aschoff.[1] These are found most frequently in the wall of the left ventricle and are composed of large, round wandering cells, which are often concentrically arranged around a small vessel. They are believed by Aschoff, Bracht and Wachter,[2] Thalhimer and Rothschild,[3] and others to be peculiar to rheumatism. In longstanding cases the Aschoff nodules are represented by sclerotic patches (Thalhimer and Rothschild). Rheumatic pericarditis

[1] Verh. d. Deut. Path. Gesellsch., 1904, viii, 46.
[2] Deut. Arch. f. klin. Med., 1909, xcvi, 493.
[3] Jour. of Exp. Med., 1914, xix, 417.

is usually fibrinous or sero-fibrinous. In many cases it is so slight as to be overlooked clinically.

In some cases of rheumatism, especially when endocarditis is also present, inflammatory nodules, varying in size from a pinhead to a large cherry, occur in relation to the deep fascia, the tendons or the periosteum. Occasionally, fifty or even a hundred of such nodules are observed.

**Symptoms.**—In many cases there are prodromal symptoms lasting for a few hours or a day or two, and consisting of general malaise, a sense of fatigue, darting pains in the limbs and soreness of the throat. Not infrequently, however, the onset is sudden and marked by the almost simultaneous occurrence of chilliness, elevation of temperature and pain in one or more of the joints.

*Arthritic Phenomena.*—The larger joints are usually affected first and those of the lower extremities somewhat more frequently than those of the upper. The knees, ankles, shoulders and wrists are most commonly attacked, but the hip and elbow joints and those of the feet and hands are often included. Indeed, no joint is immune. In the vast majority of cases several articulations are affected, some simultaneously, but others successively, for a striking feature of rheumatic inflammation is its tendency to shift from joint to joint, often disappearing in one as it attacks another. Not infrequently the same articulation is attacked two or three times before the infection is overcome.

The affected joints are painful, tender to the touch and often, although not invariably, slightly reddened. The tenderness is especially marked, and when a number of joints are involved at the same time the patient may lie absolutely motionless, every effort to change his position being attended by intense suffering. The pain is almost always worse at night. The swelling, which is usually greatest in the superficial joints, may be firm and elastic or soft and fluctuating. Not rarely the tumefaction spreads beyond the articulations to the sheaths of the tendons and even to the muscles.

*Other Manifestations.*—The *fever* is usually in relation to the severity of the arthritic symptoms, and in the majority of cases ranges between 101° and 104° F. It is irregularly remittent and atypical, lasts a variable time, and declines, as a rule, by lysis. The skin is usually bathed in *copious perspiration*, which often has a very sour odor and an acid reaction. Accompanying the sweats there is in many cases an abundant crop of sudamina. The tongue is thickly coated with a whitish fur, but the appetite frequently remains good, and the stomach is usually retentive. The bowels are constipated. Except in the rare cases of so-called cerebral rheumatism, presently to be described, the mind is, as a rule, clear. It is noteworthy, however, that delirium may occur as a result of the too free use of salicylates. The *blood* presents definite changes, which in degree are roughly parallel to the severity of the attack. The red cells and hemoglobin are almost always decreased and not infrequently the anemia is very pronounced. The number of leucocytes is increased, the count ordinarily ranging between 10,000 and 20,000. The *urine* is scanty, dark colored, of high specific gravity, and very acid. It is rich in urates, but deficient in chlorids. Sometimes it contains a small amount of albumin.

Inflammatory lesions of the *heart*, especially endocarditis, are very common, and are to be regarded as localizations of the rheumatic infection rather than as complications. *Endocarditis* occurs in at least 40 per cent. of all cases at every age, and in not less than two-thirds of the cases in children. The more severe and extensive the articular inflammation, the more likely it is to develop, although it often occurs when the other manifestations of

rheumatism are so mild and so indefinite that they attract little or no attention. The process shows a decided predilection for the mitral leaflets and in the vast majority of cases is of the benign type. Malignant endocarditis as a result of rheumatism is rare in the United States, although it is apparently not uncommon in England. In many cases the occurrence of a soft apical murmur is the only indication of the endocardial involvement. As weakening of the ventricular contractions from the toxemia may also cause a soft systolic murmur at the apex, it is not always possible to make an exact diagnosis of endocarditis until the acute symptoms have entirely subsided and the patient is up and about. *Pericarditis* is less common than endocarditis, although it is somewhat frequent in children and it is found in the large majority of all fatal cases. The exudate is almost always either fibrinous or sero-fibrinous. In virtually all cases of pronounced endocarditis or pericarditis *the myocardium* is involved to a greater or less extent. Not rarely both membranes of the heart and the myocardium are seriously involved and to this condition the term "carditis" has been applied. Myocarditis is sometimes the chief cardiac lesion and occasionally it occurs independently of any other. The usual evidences of its occurrence are progressive weakening of the cardiac impulse and sounds, increasing frequency of the pulse, extension of the area of cardiac dulness, the development of a soft apical, systolic murmur and the appearance of arhythmia in some form. In severe cases there may be also restlessness, dyspnea, cyanosis with pallor, and vomiting.

*Arterial changes* occasionally occur in acute rheumatism. The aorta, especially its arch, is most often affected and the chief alterations are in the media. Klotz[1] reports a case of aortic aneurysm in a boy of six years with rheumatic fever. *Phlebitis* is rare. In 1899 Garnier[2] collected 18 cases.

While it is generally agreed that some relation exists between *acute chorea* and rheumatism, the nature of the relation still remains to be determined. Sometimes the two diseases appear together, but more commonly one precedes the other. The frequency of the association cannot be definitely stated, as the manifestations of rheumatism in children, in whom chorea chiefly occurs, are often so slight and evanescent that a history of its absence is not always reliable. Of 2239 cases of chorea analyzed by Starr, (Nervous Diseases, Organic and Functional, 1907) 372 (16.6 per cent.) gave a definite history of rheumatism. On the other hand, of 226 cases of chorea reported by Still[3] no less than 126 (55.7 per cent.) presented evidence of rheumatism. A number of prominent English clinicians are of the opinion that acute chorea is essentially a cerebral manifestation of rheumatism, but this view is not universally accepted. It is more likely that the virus of rheumatism is only one of several infectious irritants that can produce the central disturbances which peripherally are expressed as chorea.

Rarely during the course of the disease or even after convalescence has apparently begun the grave condition known as *cerebral rheumatism* supervenes. This is a group of cerebral manifestations consisting of headache, extreme restlessness, delirium, and, frequently, coma. In some cases convulsions succeed the delirium or occur independently of it. Hyperpyrexia is often present also, but it is not a constant feature. Cerebral rheumatism is almost unknown in childhood.

In many cases acute rheumatism is preceded or accompanied by *acute tonsillitis*. While the relation of these two diseases has not been definitely

[1] Jour. Path. and Bact., 1913, xviii, No. 2.
[2] Progrès Médical, Feb. 25, 1899.
[3] Practitioner, 1901, lxvi, 53.

determined, it is probable that the tonsil is at least one of the portals through which the inciting agent of rheumatism enters the body.

English writers lay much stress upon the development of *subcutaneous nodules* as evidence of rheumatism, particularly in childhood. These bodies, usually about the size of a small pea, but sometimes as large as a hazel-nut, appear to have been first described in 1843 by Frorich.[1] They are found in the neighborhood of the joints, especially about the elbows, patellæ, and malleoli, on the sheaths of superficial tendons, and sometimes over the skull and vertebral spines. They are firm, unattached to the skin and usually painless. They grow rapidly and persist for from a few days to several weeks. They are apparently characteristic of rheumatism, but are observed less frequently in America than in England. Certain *cutaneous eruptions*, especially erythema nodosum, erythema multiforme, and urticaria, sometimes develop during the course of rheumatism. Purpura may also appear on the skin, but there is no reason to believe that so-called purpura rheumatica, or Schönlein's disease, is really a result of rheumatism.

**Course.**—The duration of rheumatism is variable. In some cases the disease terminates within ten days or two weeks; more commonly it persists for four or five weeks; and not rarely it runs on for several months, the patient's condition alternately becoming better and worse without apparent cause. Relapses are very common. In some cases the affected joints remain swollen, tender and stiff for many weeks, but permanent articular changes from acute rheumatism are rarely, if ever observed, at least in the United States.

**Subacute Rheumatism.**—In this form few joints are affected and the symptoms generally are of mild character. Complications involving the heart often occur, however, and the arthritis is likely to persist for a long period, not rarely for several months.

**Chronic Rheumatism.**—There is no reliable evidence that rheumatism ever becomes a distinctly chronic disease or ever begins as a chronic affection. The many cases of polyarthritis with a tendency to chronicity and to permanent structural changes in or about the joints, which are frequently referred to as chronic articular rheumatism, had better be regarded as examples of *rheumatoid arthritis* or *arthritis deformans*, and treated accordingly, until we possess a more accurate knowledge of their etiology and can classify them more definitely.

**Acute Rheumatism in Children.**—In young children acute rheumatism frequently declares itself less frankly than in adults. In many cases the arthritic phenomena are exceedingly mild or are entirely replaced by manifestations which in older persons are commonly regarded as complications. Thus, chorea, tonsillitis, endocarditis, pericarditis or subcutaneous nodules may be the first conspicuous feature of the infection. Arthritic pain was the chief complaint in only 24 per cent. of 500 cases analyzed by McConnell.[2] Sometimes a slight, persistent fever and increasing anemia are for a time the chief manifestations, no local features presenting themselves other, perhaps, than transient torticollis, an occasional attack of epigastric pain, or the muscular aching, frequently referred to by parents as "growing pains."

**Complications.**—Apart from the cardiac and vascular lesions, which are as much manifestations of the disease as the arthritis, complications are not common. *Hyperpyrexia* occasionally occurs, the temperature rising to 106,° 108° or even 110° F. Such extreme temperatures are almost always accompanied by severe nervous disturbances. *Pleurisy* sometimes develops,

[1] Die Rheumatische Schwiele. Weimar, 1843.
[2] Archiv of Pediatrics, Jan., 1906.

especially when there is pericarditis. *Pneumonia* may occur in association with pleurisy or as an independent condition. *Iritis*, probably as a result of the lodgement of organisms in the fine capillaries of the iris, is an exceptional complication. It was observed but once in McCrae's[1] 270 cases of rheumatism. *Acute nephritis* has been occasionally reported (Leyden, Hayem, Lees, Poynton). A few cases of *multiple neuritis* are on record. Thyroiditis, parotitis, mastitis and orchitis have been mentioned.

**Prognosis.**—Acute rheumatism rarely proves immediately fatal. The average mortality is probably less than 3 per cent. The chief danger to be apprehended during the attack is from endocarditis or pericarditis. Cerebral rheumatism is an exceedingly dangerous manifestation, but it is fortunately very rare. Occasionally death occurs suddenly from syncope or pulmonary edema, the result of myocarditis, or from embolism or thrombosis of an important intrathoracic vessel. In the large majority of cases the chief concern is in regard to the likelihood of permanent crippling of the heart and the liability to future attacks.

**Diagnosis.**—As a rule, the diagnosis of acute rheumatism is readily made. It may be difficult, however, if the infection is ill-defined or atypical or localizes itself in a single joint. The conditions with which it is most likely to be confused are secondary infectious arthritis, gout and arthritis deformans.

*Secondary Infectious Arthritis.*—The inflammation of the joints occurring in various infectious diseases, such as pyemia, scarlet fever, pneumonia, gonorrhea, cerebrospinal fever and tuberculosis may simulate rheumatic arthritis more or less closely, but careful attention to the antecedent or concomitant symptoms in the case will usually make the diagnosis clear. In contrast to rheumatism a liability to suppuration exists in the entire group. *Gonorrheal arthritis* is associated with urethritis, frequently involves joints that are rarely attacked in rheumatism, such as the sacro-iliac, sternoclavicular, temperomaxillary and intervertebral, and is accompanied by less constitutional disturbance than rheumatism. Moreover, it is prone to involve the tendon sheaths; it shows little tendency to flit from joint to joint; and is extremely resistant to salicylic medication. In doubtful cases a positive reaction with the gonococcus complement-fixation test is of value in establishing the diagnosis. A negative reaction, however, does not exclude gonorrhea. *Acute tuberculous polyarthritis* may be indistinguishable from the rheumatic form, but fortunately it is very rare.

*Gout.*—The inflammation in gout, while sometimes polyarticular, shows a decided predilection for the metarso-phalangeal and the tarsal joints; the skin over the affected parts is usually red and shiny; uratic concretions (tophi) are frequently found in the helix of the ear or in the tendons of extensor muscles; the blood contains an excess of uric acid; there is little tendency to endocarditis; digestive disturbances are commonly present; fever is not rarely absent; and eventually the affected joints become stiff and deformed. Finally, the age of the patient, his occupation, and his habits as regards eating and drinking may be suggestive.

*Arthritis Deformans.*—The diagnosis between this disease and rheumatism may be difficult at the onset. In arthritis deformans, however, certain joints are often involved that are rarely affected in rheumatism, namely, those of the cervical vertebræ, the temporomaxillary joints and the sternoclavicular joints; muscular atrophy above and below the affected joints is frequently observed; the inflammation shows little or no tendency to flit from joint to joint; the fever is usually slight and the pulse-rate high in proportion to the elevation of temperature; the salicylates have no effect other than that of a

[1] Jour. Amer. Med. Assoc., 1903, xl, 215.

mild analgesic; and permanent changes in the affected joints often appear early.

*Osteomyelitis* may lead to error, but in this condition a history of trauma may frequently be obtained; the inflammation is usually confined to a single part, most commonly the lower end of the femur, the upper end of the tibia, or the upper end of the humerus; the point of maximum tenderness is over the shaft of the bone near the joint, and the latter is involved only secondarily, if at all; the affected part is often definitely edematous over a considerable area; and the febrile process is of the hectic type and is, as a rule, ushered in with a distinct chill.

*Infantile Scurvy.*—This disease has frequently been confused with rheumatism, but the age of the patient (under 2 years) and the feeding history should always arouse suspicion. Moreover, in scurvy there is usually no fever, the swelling and tenderness are along the shafts of the bones near the joints, rather than in the joints, the gums are frequently swollen and congested, slight bleeding from the mucous membrane of the mouth and into the skin is common, and correction of the diet results in very rapid recovery.

Mistakes in diagnosis may also occur in connection with *hereditary syphilis*, *hemophilic arthritis*, and the *erythema group with acute joint symptoms;* but a careful consideration of all the circumstances of the case will usually prevent error.

**Prophylaxis.**—Much can be done to prevent the occurrence or recurrence of rheumatism by guarding the individual against exposure to cold and wet, by insisting that he be warmly clad, by increasing his resisting power through wholesome food, a daily cool bath, graduated gymnastic exercises, and, if need be, the use of iron and other tonics, and, above all, by removing any existing foci of infection in the tonsils or elsewhere.

**Treatment.**—Absolute rest in bed is essential and should be maintained, even in the absence of cardiac involvement, for at least ten days after the arthritic symptoms have completely subsided and the temperature has become normal. To guard against chilling of the body the patient should wear a loose flannel night dress and, if the weather is cool, lie between blankets. The room should be well ventilated, but free from drafts. Milk, cereals, bread and butter, eggs and light broths are suitable forms of nourishment during the febrile period. After the temperature has become normal a liberal diet, including meat, is advantageous. The free use of water and lemonade should be encouraged. The bowels should be regularly moved by mild laxatives, preferably salines. When sweating is profuse the patient is made more comfortable by drying the skin with a soft absorbent towel and then sponging it lightly with alcohol. Spraying or swabbing the throat with alkaline antiseptic solutions is desirable, but even when the tonsils are seriously affected, tonsillectomy during the course of the infection is inadvisable, unless the attack is unduly prolonged and refractory to treatment.

*Internal Medication.*—Salicylates have power to control the symptoms, but they apparently do not lessen the tendency to endocarditis. Usually about 20 grains (1.3 gm.) of sodium salicylate should be given every three hours until the pain is definitely relieved and the fever is reduced or until ringing in the ears or other untoward symptoms indicate that the limit of tolerance has been reached. Even in children from 8 or 10 years of age a dose of at least 10 grains (0.6 gm.) every three hours is advisable. The possibility of large doses causing delirium, even maniacal excitement, in susceptible persons should be borne in mind. As the pain and fever lessen the size of the dose or the frequency of administration should be reduced, but the treatment should not be discontinued until at least a week after the

disappearance of the symptoms. Alkalis, such as potassium bicarbonate, potassium citrate, or sodium citrate are also of service, for while they probably exert no influence on the rheumatism itself, they lessen the tendency of the salicylates to cause renal irritation and acidosis. The dose of the alkali should be about equal to that of the salicylate, and the two drugs may be given in combination, as in the following prescription:

℞. Sodii salicylatis.....
Potassii bicarbonatis.....āā ʒiv (15.0 gm.)
Aquæ menthæ piperitæ..... fʒvi (175.0 mils) M.

Sig.—A tablespoonful in water every three hours.

Generally speaking, sodium salicylate is the most efficacious of the salicylates and should be tried first, as a rule, in all severe forms of the disease. However, in mild attacks, or in cases in which sodium salicylate is not well borne or fails to do good, one of the esters, especially acetylsalicylic acid (aspirin) may be substituted. Salicylic acid itself is too irritant for internal use and phenyl salicylate (salol) is more poisonous and much less reliable than the sodium salt or the acetyl ester. When no salicylic compound can be tolerated by the mouth, sodium salicylate may be administered by the rectum. For an adult 2 drams (8.0 gm.) in 150 mils of thin starch water may be injected well up into the bowel after the use of a cleansing soap-suds enema, and repeated every 12 or 24 hours. Conner[1] has administered sodium salicylate intravenously with good results. He gives 15 to 30 grains (1.0–2.0 gm.) every 8 to 12 hours, using a fine needle to avoid thrombosis.

Morphin is sometimes required to relieve intense pain, subdue restlessness and procure sleep. Acetphenetidin, antipyrin, and phenylcinchoninic acid (*atophan*), in moderate doses (5 grains–0.3 gm.), are also useful adjuvants to salicylic compounds when the pain is very severe. If adynamia is marked quinin, as recommended by Garrod, Duckworth and Da Costa may prove beneficial. Anemic patients are usually benefited by iron. Indeed, when the ordinary remedies fail, syrup of iodid of iron, in large doses (1–3 drams daily), as recommended by J. C. Wilson, is sometimes effectual. Vaccines, even when prepared from the patient's own bacteria, usually fail. Daily intravenous injections of a foreign protein, such as stock typhoid vaccine, are occasionally successful, however, in refractory cases, although they not rarely cause severe reactions.

Cerebral rheumatism is best treated by cold sponging or cold baths. Moderate venesection and lumbar puncture are worthy of trial. The treatment of endocarditis and of pericarditis is considered on pages 672 and 704 respectively. The importance of prolonged, absolute rest in all cases in which the heart becomes affected cannot be overestimated. The patient should not be permitted to leave his bed for several weeks after the fever has subsided, or if tachycardia or arhythmia is present, until this has entirely disappeared, and even then the amount of his exertion should be carefully graduated, the effect on the pulse of each additional effort being used as a guide.

*Local Treatment.*—In mild cases the application of cotton-batting or lamb's wool to the affected joints will suffice. When the pain is severe compresses soaked in a saturated solution of magnesium sulphate and covered with oiled muslin often afford relief, but, as a rule, applications of methyl salicylate, diluted with 1 or 2 parts of cotton-seed oil, are more effective. A mixture of equal parts of guaiacol and glycerin is also useful. In some cases counter-irritation by means of a fly blister (2 inches square on each

[1] Medical Record, 1914, No. 8.

side of the joint) yields better results than any other form of local treatment. No matter what application is made, it is important that the inflamed joints should be kept at complete rest in a position of relaxation or moderate flexion. This may be accomplished by means of small sand bags or of padded splints and a roller bandage.

Lingering swelling often yields to an ointment of mercury, belladonna and salicylic acid with firm strapping of the articulation. The following ointment may be used:

℞. Acidi salicylici ..... ℥iss (6.0 gm.)
Unguenti belladonnæ .....
Unguenti hydrargyri ..... āā ℥iv (15.0 gm.)
Adipis ..... ℥iv (125.0 gm.) M.

In other cases venous hyperemia by Bier's method will be found efficacious. The bandage should be applied for about two hours, twice a day. It should be tight enough to cause redness but not edema. Baking with superheated air and gentle manipulation and massage are useful in overcoming persistent stiffness.

*Convalescence* must be carefully guarded. The patient should be warmly clothed, well fed, given iron and other tonics, and, if necessary and feasible, removed for a time to a more salubrious environment.

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## MUMPS

(Epidemic Parotitis)

**Definition.**—Mumps is an acute, infectious and contagious disease, characterized by inflammation of the salivary glands, especially the parotid glands, and frequently by orchitis.

**Etiology.**—Mumps is always present to a greater or less extent in cities, and from time to time becomes epidemic. Outbreaks usually occur in cold weather. The disease is highly contagious and spreads rapidly through schools and other institutions where children are closely associated. Individual susceptibility, however, is less pronounced than in many other infections and a large proportion of the population is never attacked. The disease is transmitted chiefly by direct contact, and rarely, if ever, through fomites or a third person. The infectious agent apparently is contained in the saliva and is transferred from one person to another by mouth spray expelled in talking, coughing or sneezing. The period of communicability probably begins before the occurrence of the parotid swelling and continues for some time after the disappearance of all symptoms.

The causative organism has not been isolated, but it seems to be of the filterable type. Martha Wollstein[1] and others have succeeded in producing the chief lesions of the disease in animals by means of filtered extracts of saliva secured from persons suffering from infectious parotitis.

The age incidence of mumps reaches its maximum between the fifth and fifteenth years. While no age is exempt, the disease is very uncommon in the extremes of life. Males and females are about equally affected. One attack usually confers lifelong immunity.

**Morbid Anatomy.**—Very little is known of the minute changes which the parotid glands undergo in mumps, as there is seldom an opportunity for investigating them. When the disease is produced experimentally in

[1] Jour. Exp. Med., 1916, xxiii, 353.

animals, however, the lesions consist of catarrhal inflammation of the ducts and of acute interstitial inflammation of the gland itself. Apparently, the periglandular tissues are also the seat of more or less inflammatory edema. Suppuration is very rare and always the result of secondary infection with pyogenic organisms.

**Symptoms.**—The *period of incubation* is usually about 18 days, and is rarely more than three weeks or less than two weeks. Languor, chilliness, and slight fever sometimes precede the local signs by a day or two, but more frequently the initial symptoms are aching, tenderness and swelling in the parotid region. One gland only may be involved, but, as a rule, the other becomes affected after the lapse of twenty-four or forty-eight hours or, in exceptional cases, of a week. The swelling commonly fills the space between the mastoid process and the jaw and extends in front of the ear, the lobe of which is elevated, over the cheek and downward some distance into the neck, producing in severe cases a most grotesque appearance. Generally it has a doughy consistence, but it may be firm. Pressure elicits tenderness. The skin over the gland usually retains its normal color, although occasionally there is slight redness. The inflammation sometimes extends to the submaxillary or sublingual glands, or rarely attacks one or the other of these glands instead of the parotids. Internally, the edema may spread to the fauces and tonsils.

In all cases there is more or less local discomfort. The movements of the jaw are impeded and mastication, deglutition and even speaking may be painful. Swallowing of acid substances, such as vinegar or lemon-juice, by exciting a reflex flow of saliva, increases the pain. The salivary secretion may be increased or diminished. Tinnitus aurium and deafness are occasional symptoms.

The temperature during the attack usually ranges between 100° and 102° F., but exceptionally it is much higher. The blood shows, as a rule, both a relative and an absolute lymphocytosis, with a decrease of the polymorphonuclear forms. The total number of leucocytes may be slightly increased or decreased, or about normal. Even in the absence of any symptoms pointing to a secondary involvement of the meninges, the cerebrospinal fluid may also show lymphocytosis (Monod,[1] Feiling[2]).

In the majority of cases the parotid swelling reaches its height by the fourth or fifth day, and than rapidly subsides along with the constitutional symptoms, the whole process rarely occupying more than one or two weeks. Occasionally very light attacks occur in which there is neither pain nor constitutional disturbance and the swelling disappears within three or four days. Resolution is almost always complete, but occasionally induration of the gland ensues, and in a few instances abscess and even gangrene have been observed as a result of secondary infection. In exceptional cases a *relapse* occurs after an interval of two, three or even four weeks.

**Complications.**—A peculiar feature of mumps is its tendency to excite inflammation of the sexual glands, especially the testicle. The *orchitis* usually occurs at the height of the disease or during the period of decline, although it may develop after the parotid swelling has entirely disappeared. It is commonly regarded as a true metastasis, but it is more probably a direct result of the systemic infection, in as much as the testicle is occasionally affected before the parotids and in some epidemics a few cases have been observed in which the orchitis was the only lesion. The frequency of orchitis varies in different outbreaks from 1 to 40 per cent. The incidence of

[1] Lancet, July 12, 1913.
[2] Thése de Paris, 1902.

testicular involvement was 18 per cent. in 18,153 cases of mumps collected from various sources by Wesselhoeft.[1] The process is uncommon before puberty and usually involves but one testicle. Ringberg[2] found the disease bilateral in only 33 of 279 cases of orchitis in epidemic parotitis. The inflammation ends favorably, as a rule, in the course of a week or ten days, although atrophy of the gland is a somewhat frequent sequel. Even when the atrophy is bilateral, however, procreative power is not invariably lost. Occasionally, the onset of orchitis is marked by high fever and delirium.

In females the *ovary*, *mammary gland*, and *external labia* are exceptionally attacked in the same way as the testicle in the male. Other glands, such as the *lachrymal*, *thyroid*, and *prostate*, may also become swollen and tender, and very rarely urethritis supervenes. *Acute pancreatitis* is not an uncommon complication, but it is usually mild, eventuating in recovery. *Swelling of the cervical lymph-nodes is* sometimes observed.

*Deafness* may occur from catarrh of the middle ear or labyrinthine disease; in the latter case it is likely to develop abruptly and to prove irremediable. Inflammatory affections of the eye—*conjunctivitis*, *keratitis*, and *iritis*—have been reported in some epidemics. According to Antonelli[3] 18 cases of *optic neuritis* due to mumps had been reported up to 1903. This condition may result in optic atrophy. Cerebral complications are sometimes observed, the most common being *meningitis* or *meningo-encephalitis*. In 1913 Acker[4] collected from the literature 29 cases of meningitis and reported 2 additional ones. Recovery is the rule in such cases, but occasionaly paralysis or aphasia remains as a sequel. *Lesions of the cranial nerves*, including facial palsy, and *polyneuritis* are said to have occurred.

In 1851 Burne[5] put on record a case of *acute nephritis* following mumps and since then at least 40 additional cases have been reported. Jaccoud, Marfan, and Taschner[6] mention the occurrence of *endocarditis*. *Polyarthritis* is another rare complication.

**Diagnosis.**—The disease is, as a rule, readily recognized. In *secondary parotitis* there is evidence of the primary condition of which the parotid inflammation is but a complication and the process develops more slowly than in mumps, is nearly always unilateral, and is prone to suppuration. In *acute cervical adenitis* the center of the swelling is below the ramus of the jaw, the course is prolonged and suppuration is common.

**Prognosis.**—The prognosis is favorable. Death is rare, and when it occurs is usually the result of meningitis, nephritis or gangrene. There were only 7 deaths in Ringberg's[7] 58,381 cases.

**Prophylaxis and Treatment.**—Prophylaxis consists in isolation of the patient for four weeks from the onset of the disease; the exclusion of other children of the household from school and other public gatherings for at least three weeks after exposure to infection; and disinfection of the secretions from the nose and mouth and of all articles soiled therewith.

**Treatment.**—The patient should be confined to bed and, as mastication is painful, given a diet of soft, bland food. A mild aperient may be administered at the beginning of the attack. In mild cases protection of the affected glands with cotton-batting will be sufficient local treatment. If the pain is severe several thicknesses of gauze wrung out of a saturated solution

[1] Boston Med. and Surg. Jour., Oct. 7, 1920.
[2] Ugeskr. f. Läger, 1896, 5 R, iii, 5.
[3] Archives d'Ophthalmologie, Oct. 1903.
[4] Amer. Jour. Dis. of Child., 1913, vi, 399.
[5] Prov. Med. and Surg. Jour., 1851.
[6] Wien. med. Woch., 1904, No. 31.
[7] *Loc. cit.*

of magnesium sulphate may be applied and covered with oiled muslin, or an ointment of guaiacol (5–10 per cent.) or of ichthyol (10–20 per cent.) may be used. Small doses of acetphenetidin or of codein may be necessary.

Orchitis is best treated by elevating the testicle and applying an ointment of guaiacol (10–20 per cent.) or of ichthyol (20 per cent.). Strapping is inadvisable. Applications to either the parotid gland or testicle should be made without friction or massage.

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## WHOOPING COUGH

(Pertussis)

**Definition.**—Whooping cough is a specific, infectious and contagious disease, with an average duration of from 6 to 8 weeks, and characterized by catarrh of the respiratory tract and paroxysms of spasmodic cough, which usually end in a long sonorous inspiration, termed a whoop, and which frequently result in vomiting.

**Etiology.**—Whooping cough occurs epidemically throughout the world, and is endemic in virtually all large cities. Epidemics are more severe, but probably not more common, in winter and spring than in summer, and are not infrequently associated with outbreaks of measles. Race, sex, and social position exert no influence on the occurrence of the disease. Age, however, is an important factor. While whooping cough may occur at any period of life, and in rare instances may even be congenital, the large majority of cases occur between the ages of 6 months and 7 years. At least 20 per cent. of the cases occur in the first year and 50 per cent. between the first and fifth years. Adults are rarely affected. Individual susceptibility is very pronounced, probably being exceeded only by measles, chicken-pox and small-pox.

The disease is highly contagious, and the site both of the egress and ingress of the virus is apparently the upper respiratory tract. Transmission is effected chiefly by direct and comparatively close contact with typical or atypical cases and probably through mouth spray or droplet infection. Whether carriers play any part in the spread of the disease is not definitely known. Conveyance of the virus by fomites or by a third person seems to be possible, but it is certainly exceptional. The period of maximum infectivity is generally believed to be in the catarrhal stage. One attack usually confers immunity for a life time.

The *exciting cause* of whooping cough is probably the hemoglobinophilic bacillus described by Bordet and Gengou[1] in 1906. This organism closely resembles in its morphology the influenza bacillus, but it is somewhat larger. It is agglutinated by the serum of convalescents from whooping cough, although with considerable inconstancy, and gives rise to a specific antibody which makes possible complement fixation. Some authorities still maintain, however, that all of Koch's postulates have not been fulfilled.

**Morbid Anatomy and Pathogenesis.**—There are no characteristic lesions. The usual changes consist of catarrhal inflammation of the upper respiratory tract, especially of the larynx and trachea, and of more or less swelling of the bronchial lymph-nodes. Lesions of various complicating conditions, such as emphysema, bronchiectasis, broncho-pneumonia, atelectasis, cerebral hemorrhages, and dilatation of the heart, may also be found.

[1] Ann. de l'institut Pasteur. 1906. xx, 731.

The epithelium of the respiratory tract may be damaged mechanically by the bacilli themselves, which, according to Mallory[1] and his co-workers, are present in enormous numbers between the cilia of the cells, or by the action of a specific toxin. As the catarrhal condition does not seem sufficient of itself to account for the severe paroxysms of cough, it is possible that a toxin produced by the causative agent enters the blood and increases through a selective action the excitability of the terminal filaments of the vagus or of the cough center in the medulla.

**Symptoms.**—The *period of incubation* varies in length from two days to two weeks, the average being about four or five days. The symptoms are usually divided into three stages, although, of course, such a division must be more or less artificial.

*Catarrhal Stage.*—The disease usually begins like an ordinary cold with chilliness, suffusion of the eyes, lachrymation, sneezing, a dry cough, and sometimes slight fever, especially at night. Even at this period suspicion may be aroused by the great frequency of the cough and its tendency to occur in paroxysms. The duration of this stage is usually from 1 to 2 weeks, but it may be only two or three days.

*Paroxysmal Stage.*—The cough during this stage is very severe, and frequently so distressing that the child, feeling its approach, seeks some person or object near him for support. Each paroxysm begins with a rapid succession of short expiratory efforts of an explosive character and without intervening inspirations. The expiratory efforts commonly continue so long that the face becomes swollen and cyanotic, the veins of the neck become distended, the eyes prominent and watery, copious perspiration breaks out, and suffocation seems imminent. In a few seconds, however, there follows a long-drawn inspiration accompanied by a peculiar noise, which has been likened to a whoop. Usually the whole process is repeated several times and at last is terminated by the expectoration of a variable quantity of viscid mucus and very often by vomiting. In violent fits of coughing the urine or feces may be discharged involuntarily, or blood may escape from the nose or mouth or be extravasated beneath the conjunctiva. It must be borne in mind that while the whoop is characteristic it is not always present. It is not often observed in young infants; it may be absent in older children if the seizures are very mild; and it frequently disappears upon the development of severe pulmonary complications.

The paroxysms last from a few seconds to more than a minute and vary in frequency from 3 or 4 a day to 2 or 3 an hour, being almost always more numerous at night. A close atmosphere, physical exertion, loud speaking, eating, or emotional excitement of any kind tends to precipitate them. Between the paroxysms there is often little or no indisposition, unless some complication is present. In severe cases, however, the puffiness of the face persists, and sometimes considerable exhaustion ensues as a result of vomiting and loss of sleep. The duration of the paroxysmal stage is usually about four weeks, but it may be shorter or much longer than this.

In uncomplicated cases there is little or no fever. Physical examination of the chest reveals nothing abnormal, except, perhaps, the presence of a few râles, and during the paroxysms some diminution of the vesicular murmur. Occasionally, a small ulcer is produced on the frenum of the tongue as a result of abrasion by the lower incisor teeth. In severe attacks the urine may be slightly albuminous. Pronounced leucocytosis (15,000–30,000) with an increase of lymphocytes and a relative decrease of polymorphonuclear

[1] Jour. Med. Research, 1912–13, xxii, 115, 391.

forms is an almost constant feature. It begins in the catarrhal stage and attains its maximum in the paroxysmal stage.

*Terminal Stage.*—This period, which usually lasts three or four weeks, but may be prolonged to several months, is marked by a very gradual improvement in all the symptoms. The cough becomes more loose and the paroxysms diminish in frequency and severity and finally cease entirely.

**Complications.**—These are many and, as a rule, more serious than the disease itself. *Bronchopneumonia* is common in infants and young debilitated children, and is responsible for most of the deaths. *Collapse of the lung* frequently occurs in association with bronchopneumonia, and if it involves a large area, it causes intense dyspnea and sometimes sudden syncope. *Vesicular emphysema* is always present to a greater or less extent in severe cases, but it rarely remains after the disappearance of the cough. Rupture of the lung with the production of *pneumothorax* or *subcutaneous emphysema* has occurred. *Pleurisy* is an occasional complication. *Tuberculosis* is sometimes reactivated by whooping cough.

*Hemorrhages* may take place in various parts of the body, particularly into the conjunctiva or from the nose; even bleeding into the skin has been observed. Albuminuria is not uncommon, but actual *nephritis* is rare. *Dilatation of the heart* may occur, especially if there has been any preexisting myocardial weakness.

*Vomiting* may be so persistent as to constitute a serious complication and lead to exhaustion and emaciation. In delicate children *diarrhea* sometimes supervenes. *Stomatitis* is often seen in severe cases, and in poorly nourished children it is occasionally of the gangrenous type (cancrum oris). As a result of the violence of the cough, *prolapse of the rectum* or *hernia* may occur.

Nervous complications rank next in importance to those of the respiratory tract. *Convulsive disturbances* are not very uncommon. They may take the form of twitching of the facial muscles, spasm of the larynx, or epileptiform seizures. Valentine[1] in 1901 collected 79 cases of *paralysis* occurring during pertussis. In 40 there was hemiplegia; in 16, monoplegia; and in 5 or 6 paraplegia. In 64 cases death resulted in 14; permanent paralysis in 22, and recovery in 28. Paralysis is usually due to hemorrhage into the brain or meninges. In a few cases *acute encephalitis* has been observed. Eshner[2] has collected 6 cases of *peripheral neuritis*. In a few instances *blindness* or *deafness*, temporary or permanent, has occurred. Möbius, Neurath and others have cited examples of *melancholia* following whooping cough.

Finally, other acute infectious diseases, especially measles, rubella, scarlet fever or diphtheria, may be associated with pertussis.

**Diagnosis.**—Before the occurrence of the whoop it may be difficult or even impossible to distinguish whooping cough from *ordinary bronchial catarrh*, but suspicion should be aroused if the cough is persistent, paroxysmal and worse at night, is followed by vomiting, and is out of all proportion to the degree of catarrh; if lymphocytosis is present; and if there are other cases of pertussis in the house or neighborhood. *Enlargement of the tracheal or bronchial lymph nodes* may give rise to a hard spasmodic cough, but in this condition, which is essentially chronic, there is no evidence of contagion, the cough lacks the inspiratory whoop and rarely ends in vomiting, leucocytosis with a preponderance of lymphocytes is absent, and the complement-fixation test for pertussis is negative.

**Prognosis.**—Whooping cough is usually well borne by healthy children over 3 years of age, but it is a serious disease in infants and in delicate

[1] Thèse de Paris, 1901.
[2] Jour. Amer. Med. Assoc., Jan. 10, 1903.

children under the age of 6 years. The general mortality is from 3 to 10 per cent. In infants the death-rate may be as high as 25 per cent. or higher. In analysis of 6868 cases, Luttinger[1] found that 97 per cent. of the deaths were in children under 6 years of age.

**Prophylaxis.**—This consists in separation of the patient from susceptible children, especially infants, and his exclusion from school and from public gatherings for six weeks or until the whoop has disappeared, and the disinfection or destruction of the patient's expectoration and vomitus and of all articles soiled therewith. Vaccines have been used with some success. An injection should be given weekly for three weeks, the average dose for a child being 1000 million bacilli and for an adult, 2000 million bacilli.

**Treatment.**—An abundance of fresh air and sunlight, protection from changes of weather, and a light but nutritious diet are important elements of treatment. During the catarrhal stage it may be advisable to keep the patient in his room or even in bed, but later, if the weather is favorable, he need not be confined indoors. A change of air, especially to the seashore, is often a valuable aid in protracted cases. If vomiting is very frequent, it is important to give small feedings, preferably of liquids, immediately after the paroxysms. Occasionally it may be necessary to use predigested foods or to have recourse to nutritive enemas.

The drugs of most value in lessening the severity and frequency of the paroxysms are belladonna, antipyrin, and bromids. Belladonna to be effective must be given in doses sufficient to produce flushing of the cheeks and dilatation of the pupils. To a child of 2 years 2 minims (0.12 mil) of the tincture may be given three or four times a day, and the dose gradually increased until the physiologic effects of the drug are evident. The dose being taken when the limits of toleration are reached should be maintained for a considerable period. Antipyrin, in doses of 2–3 grains (0.13–0.2 gm.) every three of four hours for a child of 2 years, is sometimes very efficacious. Bromid or sodium or potassium, in doses of 5 grains (0.3 gm.) three times a day, for a child of two years, is also useful. It may often be combined advantageously with antipyrin or belladonna, as in the following formula:

℞. Sodii bromidi ..... ʒi (4.0 gm.)
Antipyrinæ ..... gr. xxx (2.0 gm.)
Glycerini ..... fʒi (4.0 mils.)
Aquæ menthæ piperitæ ..... q. s. ad fʒiii (90.0 mils) M.
Sig.—A teaspoonful in water three or four times a day for a child of 3 years.

Benzyl benzoate sometimes affords relief, but it often fails. Ten to fifteen minims (0.6–1.0 mil) of a 20 per cent. emulsion may be given in milk or sweetened water four times a day.

Vaccines of the Bordet-Gengou bacillus have been used to a greater or less extent, but their curative value is somewhat doubtful. However, as they are apparently harmless they may be tried in severe cases. Four injections may be given with one day intervening between each. The first dose being 1 billion, the second 2 billion, the third 4 billion and the fourth 6 billion.

Chloral or codein are sometimes required at night to produce sleep. If the seizures are very violent, chloroform (a few drops on a handkerchief) may be given by inhalation. The inhalation of volatile antiseptics is undoubtedly of service in some instances. For this purpose compound tincture of benzoin, creosote, or eucalyptol may be vaporized in a croup kettle or inhaled from a respirator worn over the nose and mouth. For the relief of vomiting the application of an elastic abdominal belt has a well-deserved reputation.

[1] Amer. Jour. Dis. of Child., 1916, xii, 290.

The belt recommended by Kilmer[1] is made of linen, with a strip of elastic webbing, two inches wide, inserted on each side. It extends from the axillæ to the pubes and laces in the back.

During convalescence tonics—iron, quinin, strychnin, and cod-liver oil—are frequently required.

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## GLANDULAR FEVER

### (Acute Epidemic Infectious Adenitis)

**Definition.**—Glandular fever is an infectious and moderately contagious disease, characterized by a sudden onset and an acute course, with fever and inflammatory swelling of the lymph-nodes, especially those of the cervical region.

The disease was first described by E. Pfeiffer in 1889.[2] Whether it is a nosological entity is somewhat doubtful.

**Etiology.**—Glandular fever occurs chiefly in children between the ages of 12 months and 10 years, although in some outbreaks most of the cases have been in adults. Epidemics are most common in the winter and spring. The disease is undoubtedly contagious, but apparently intimate contact is required for transmission and receptivity is somewhat limited. The causative agent has not been isolated. Both its ingress and egress are probably by way of the upper respiratory tract.

**Symptoms.**—The onset is usually sudden with chilliness, headache, muscular soreness, sore throat, and pain in the neck, especially on motion. Nausea or vomiting may also be present. The temperature rises rapidly to 102°–104° F., continues high for from 2 to 7 days, and then falls by lysis. Pain on swallowing and redness of the throat are frequently observed, and not rarely there is also coryza. Usually by the second day the cervical lymph-nodes, especially those along the posterior border of the sternocleidomastoid muscle, become enlarged and tender. Eventually the swelling may reach the size of a pigeon's egg. The affected nodes do not fuse, but remain discrete, and suppuration is rare. Later, the axillary and inguinal nodes may become swollen, and not infrequently substernal pain and spasmodic cough suggest that the bronchial nodes are also involved. The bowels are usually constipated and the spleen is often palpable. A moderate leucocytosis (15,000 to 20,000) is the rule, the excess of white cells being due almost entirely to mononuclear forms, many of which show bilobed Riedel nuclei.

**Complications** are rare, the most frequent being acute nephritis. Suppuration of the affected lymph-nodes and otitis media have also been mentioned.

The **prognosis** is good. According to Tidy and Morley[3] only 4 fatal cases have been recorded. As a rule, the fever subsides within a week and the adenitis within two or three weeks. The *diagnosis* is usually easy, the characteristic features being swelling of the lymph-nodes and pronounced fever without obvious cause, the disproportion between the degree of adenitis and that of the pharyngeal catarrh, mononuclear leucocytosis, and the very slight tendency to suppuration. Mumps and scarlatina are rarely confusing. Acute lymphatic leukemia may usually be excluded by the mild course,

[1] New York Med. Jour., 1903, lxxvii, 1101.
[2] Jahrb. f. Kinderheilk., 1889, xxix, 257.
[3] Brit. Med. Jour., Mar. 26, 1921.

absence of hemorrhages, moderate leucocytosis, and the presence of many white cells with bilobed nuclei.

**Treatment.**—Isolation, rest in bed, a light diet, and initial calomel catharsis are all that are required.

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## ACUTE POLIOMYELITIS

(Acute Infantile Spinal Paralysis)

**Definition.**—Acute poliomyelitis is an infectious and communicable disease, occurring in epidemics and sporadically, affecting chiefly children, characterized anatomically by inflammatory changes in the central nervous system, involving particularly but not exclusively the anterior horns of the spinal cord, and manifested clinically by constitutional disturbances of short duration and an acute atrophic paralysis of various muscles, the paralysis at its height being always in excess of what remains at the end of a few weeks or months.

The disease seems to have been first recognized by Underwood[1] in 1774, but the credit of establishing it as a distinct affection belongs to Heine, who described it in 1840 as spinal infantile paralysis. In 1843 Colmer[2] referred to an epidemic in West Feliciana, Louisiana, and since that time there have been epidemics widely scattered over the civilized world. Outbreaks have been more frequent in the last two decades, the most severe visitations having occurred in Northern Europe, especially in Norway and Sweden, in Australia and in the United States. More than 10,000 cases were reported in the United States in the years 1910 and 1911, and in 1916 an outbreak of unprecedented severity swept over the Middle and New England states, affecting more than 30,000 persons.

**Etiology and Pathogenesis.**—The vast majority of both sporadic cases and those in epidemics occur during the spring, summer and autumn, although the disease does not entirely disappear during the winter. Outbreaks may occur simultaneously in several isolated districts or they may begin in one locality and spread along the usual lines of communication. Density of population seems to have but little influence upon epidemics, more cases occurring in suburban and rural communities than in the crowded quarters of cities. The great majority of those attacked are children under the age of six years, but older children and even adults are not wholly spared, especially when the disease is present in epidemic form. The robust are as susceptible as the weak. The sexes are about equally affected. Single cases in a household are the rule, but multiple ones are by no means rare.

Although poliomyelitis is undoubtedly contagious, it is not highly so, otherwise instances of multiple cases in households would be much more common. Epidemics vary much in severity, but are, as a rule, of comparatively short duration, because many individuals in every community are insusceptible. At times the virus becomes so attenuated that only those who are highly susceptible suffer, hence there are periods in which the disease is sporadic rather than epidemic. The nature of the virus is not definitely known. It is undoubtedly a living organism, however, for Landsteiner and Popper,[3] Flexner and Lewis[4] and others have shown that it can be trans-

[1] Treatise on the Diseases of Children.
[2] Amer. Jour. Med. Sci., 1843.
[3] Zeitsch. f. Immunitätsforschung, 1909, ii, 377.
[4] Jour. of the Amer. Med. Assoc., 1909, liii, 1639.

mitted through an indefinite number of monkeys. It is present in the nasal and buccal secretions of infected persons, is eliminated in some cases by the intestines, and can be isolated from the brain and spinal cord. It is filterable and therefore ultramicroscopic; it is not readily destroyed by cold or drying; and is capable of producing the disease in monkeys even when applied to the intact mucous membrane of the nose.

The manner in which acute poliomyelitis is naturally communicated is not certainly known. The experiments of Flexner, of Kling, Wernstedt and Pettersson,[1] and of others, however, seem to justify the conclusion that the infection is usually transferred directly from person to person, and that the nasopharynx is the chief point both for the ingress and the egress of the inciting agent. Abortive cases probably play an important part in the spread of the disease. Healthy carriers of the virus also occur, but there is no precise information as to how common they are. Flexner and Amoss[2] conclude from their experiments that the virus is present in the nasopharynx in cases of poliomyelitis chiefly in the first days of illness, that with rare exceptions it diminishes rapidly as the disease progresses, and that it is uncommon for a carrier state to be developed. At one time certain experiments seemed to show that biting insects, especially stable flies, might be at least one factor in transmitting the virus, but later studies failed to confirm the earlier ones. The possibility of the domestic fly being a potential mechanical carrier of the infection does not seem to have been entirely excluded.

Having gained access to the nasopharynx of a susceptible person, the organisms penetrate to the brain and spinal cord, probably by way of the lymphatics of the nerve sheaths. The *period of incubation* is a variable one. While it is usually about a week, it may be as short as 2 days or as long as two weeks.

**Morbid Anatomy.**—The virus of acute poliomyelitis has a selective affinity for the central nervous system and affects most intensely, as a rule, the anterior gray matter of the spinal cord, although the meninges, the gray matter of the cortex, of the bulb, and of the brain stem, and even the white matter may all be affected. The process is an acute inflammatory one, involving the vessels, supporting tissue and ganglion cells. Macroscopically, the meninges and the substance of the brain and cord are congested, and a transverse section of the cord often shows softening and hemorrhages in the gray matter of the anterior horns. Microscopically, the vessels both in the white and gray matter are dilated; the outer walls of the vessels, the pia-arachnoidal membrane following the vessels into the cord and medulla, the gray matter, and in exceptional cases, the white matter are infiltrated with small mononuclear cells (lymphocytes); and many of the ganglion cells are degenerated or destroyed. In the brain the interstitial lesions are often well marked, but the nerve-cells usually escape serious injury.

Proliferation of the neuroglia follows upon the disappearance of the ganglion cells and in the course of time sclerotic contraction ensues with diminution in the size of the anterior horns. The motor nerve-fibers proceeding from the affected ganglion cells present the usual evidences of secondary degeneration and the paralyzed muscles, those of simple atrophy or of atrophy with lipomatosis.

In early cases, the most conspicuous changes outside of the central nervous system consist of slight hyperplasia of the lymphoid tissues throughout the body, enlargement of the spleen with prominence of the Malpighian

[1] Zeitsch. f. Immunitätsforsch., 1912, xii.
[2] Jour. Exper. Med., 1919, xxix, No. 4.

bodies, and focal necrotic lesions in the liver resembling those in typhoid fever. The liver and kidneys may also show cloudy swelling.

**Symptoms.** *Ordinary or Spinal Form.*—The symptoms are those of a general infection with localization in the gray matter of the spinal cord, especially in the anterior horns. The onset is sudden and usually marked by fever (100°–103° F.), irritability, general hyperesthesia, and drowsiness. Vomiting occurs in about one-third of the cases. Less frequently, diarrhea, sore throat, and aching in the head, back and limbs are also present. Convulsions are occasionally observed and in some epidemics sweating has been a prominent feature. The mind is, as a rule, clear, even at the height of the disease, although persistent drowsiness is common. After the general symptoms have lasted from 12 hours to 3 or 4 days paralysis supervenes, muscular weakness first appearing and increasing in degree and extent over a period of several days. The distribution of the paralysis varies with the site of the central lesions. The constitutional disturbances usually subside within a week and in some cases are so slight and transient as to escape notice.

The paralysis, which is almost always flaccid, affects most frequently one or both legs, but it may affect one or both legs and an arm, or all four extremities, and even muscles of the neck, trunk, and abdomen. The arms alone are rarely attacked. With complete loss of power there is usually at first a loss of all electrical contractility in the affected muscles, but in the course of a week or two galvanic contractility returns, and with it the reactions of degeneration appear. Except at the onset, when there is considerable meningeal irritation, the deep reflexes are almost always abolished in the paralyzed limbs. An increase of the patellar reflex, however, may be observed in an otherwise healthy leg, if the other leg is affected, if an arm is paralyzed, or if the bulb is involved. In very rare instances the knee-jerk is exaggerated in paralyzed and wasted legs, owing probably to an involvement of the pyramidal tracts.

Pain in the muscles and joints of the affected limbs is present, especially on handling, in a large proportion of cases and may last into the second week. Cutaneous sensibility is at no time impaired and trophic lesions of the skin, such as decubitus, are never observed, but the paralyzed members are usually cool and more or less livid. Except for a brief period at the onset in some cases, the functions of the bladder and rectum are not disturbed. Fluid obtained by lumbar puncture shows changes, which, although not absolutely characteristic, are often helpful in diagnosis. It is usually under increased pressure, clear or slightly opalescent, sterile, poor in fibrin, and moderately rich in cells (average 50 to 100 per cubic millimeter), chiefly of the mononuclear variety. In addition, it reduces Fehling's solution, frequently contains an excess of globulin-albumin, and not rarely yields a colloidal gold reaction. Examination of the blood during the paralytic stage usually shows a leucocytosis (average 18,000) with a preponderance of polymorphonuclear forms (Peabody, Draper, and Dochez[1]).

After a variable period, usually 2 or 3 weeks, the loss of power gradually recedes and occasionally complete recovery occurs. As a rule, however, the paralysis does not entirely disappear but persists in one or two extremities or certain group of muscles; most frequently in one leg, especially in the dorsal flexors of the foot or extensors of the knee, sometimes, however, in both legs, and more rarely in one or both arms. No decided improvement in the affected members is to be expected after the lapse of a year or a year and a half. Muscles destined to remain permanently paralyzed

[1] A Clinical Study of Acute Poliomyelitis, Monograph of the Rockefeller Inst. for Med. Research, June 1, 1912, No. 4.

soon show pronounced atrophy and after a year or more lose all electrical contractility.

In children even the bones may cease to grow and the shortening may eventually amount to several centimeters. In many cases after the paralysis has lasted a year or two considerable deformity ensues in consequence of the weight of the diseased part and the overcontraction of unantagonized muscles. The most common deformity is talipes equino-varus. Subluxations of the joints, the result of relaxation of the ligaments, are occasionally observed.

*Polioencephalitis* (*Poliomyeloencephalitis*).—In the majority of epidemics cases are observed in which, with or without the usual spinal symptoms, paralysis of one or more of the cranial nerves occurs. In some of these cases the paralysis begins in the legs, then extends to the trunk and arms, and finally affects the muscles innervated from the bulb, thus producing a symptom-complex identical with that of the ascending type of Landry's disease. Less frequently, the extension of the paralysis is from above downward as in the descending type of Landry's disease. In other instances the bulb or the pons bears the brunt of the attack (*bulbar* or *pontine form*) and in consequence difficulty in deglutition and articulation, dyspnea, facial paralysis, strabismus, ptosis, ophthalmoplegia, etc., occur singly or in various combinations. Occasionally a pure *encephalitic type* is observed, the paralysis taking the form of hemiplegia and the affected members eventually becoming rigid. The general symptoms of polioencephalitis simulate those of acute meningitis, and consist of moderate fever, headache, hyperesthesia, rigidity of the neck, and sopor. Vomiting and convulsions sometimes occur and not rarely there is delirium.

In some instances of poliomyelitis the symptoms of meningeal involvement overshadow all the other phenomena of the disease (*meningitic type*), and rarely a meningitis seems to be the only important lesion, paralytic features being slight and fleeting. Wickham and many other writers refer to a *polyneuritic form* with pains in the extremities as the most obtrusive feature. It is doubtful, however, whether a peripheral neuritis actually exists in such cases, the nerve-trunks themselves are not especially tender and the pains are greatly relieved by lumbar puncture.

*Abortive Form.*—Since the publication of Wickham's[1] studies on epidemic poliomyelitis in Sweden in 1905–06 it has been generally recognized that many cases of the disease run their course without definite signs of paralysis. These abortive cases are characterized by the usual fever, headache, backache, slight rigidity of the neck, vomiting, constipation or diarrhea, a general increase of reflexes, and unsteadiness of gait. Muscular weakness is sometimes observed, but it is slight and transitory. The whole course of the disease is usually less than a week. The resemblance to meningitis or even to influenza may be very close and the diagnosis only suggested by the epidemic prevalence of poliomyelitis in its typical form. The incidence of abortive cases without paralysis varies in different epidemics and at different periods in the same epidemic. It may reach 65 per cent.[2] Abortive cases doubtless play an important part in the spread of the disease.

*Sporadic Form.*—There is no essential difference between the sporadic and epidemic forms of poliomyelitis, but the communicability of the infection is less and the death-rate is lower in the former than in the latter. On the other hand, complete recovery without residual paralysis is seen more frequently in epidemic than in sporadic cases.

**Diagnosis.**—Except in epidemics or in the case of persons previously exposed to the infection, the diagnosis is not possible before the appearance

[1] Beiträge z. Kenntniss der Heine-Medinschen Krankheit, Berlin, 1907.

[2] Report of Harvard Inf. Paralysis Com., Bost. Med. and Surg. Jour., Aug. 11, 1921.

of paralysis. Cases with cerebral involvement may readily be confused with *cerebrospinal fever*, but from this disease poliomyelitis may usually be distinguished by the early occurrence of flaccid paralysis, the early abatement of the cerebral symptoms and the results of lumbar puncture, fluid obtained in this way being clear or only slightly opalescent, moderately rich in mononuclear cells and apparently sterile. In *tuberculous meningitis* the onset is usually insidious, there is gradually increasing stupor, muscular paralysis develops late, if at all, and the cerebrospinal fluid, while it may closely resemble that of poliomyelitis cytologically and chemically, contains as a rule, tubercle bacilli. The diagnosis of *epidemic encephalitis(lethargic encephalitis)* from the pontobulbar type of poliomyelitis may be impossible. In the former, however, the onset is usually somewhat gradual, progressive lethargy is a salient feature in the large majority of cases, and ocular palsies (diplopia, ophthalmoplegia, ptosis, etc.) are especially common, while paralysis of the extremities is rare.

*Acute myelitis* may be recognized by the presence of anesthesia, persistent incontinence of urine and feces, and the tendency to bed sores. The *cerebral paralyses of childhood* are spastic, are attended by exaggerated reflexes and are not followed by rapid wasting. Only in the comparatively rare encephalitic type of poliomyelitis is the paralysis spastic. When the pain in the limbs is severe *multiple neuritis* may come into question, but in this affection the onset is less acute, the sensory disturbances are more persistent, the peripheral nerves themselves are especially tender, which is not the case in poliomyelitis, and the paralysis develops more gradually, is more marked in the distal than in the proximal parts of the limbs, and is usually symmetrical.

Poliomyelitis is sometimes simulated by *scurvy* with pseudoparalysis, but in the latter there is a history of faulty feeding, other signs of scurvy are present, the disability develops gradually, and movement of the affected limbs is possible, although it is made reluctantly. In *rickets* there is sometimes pronounced muscular weakness, but there is no actual paralysis and in place of the constitutional disturbances of poliomyelitis there are enlarged fontanelles, head-sweating, distended abdomen, alterations in the shape of the chest and various other skeletal deformities. In *myatonia congenita* (Oppenheim) a pseudoparalysis occurs, but in this disease the muscular weakness is observed within a few days or weeks after birth; it is not preceded by fever or other evidences of acute infection; it is symmetrical; and is not accompanied by actual atrophy or the reaction of degeneration.

**Course and Prognosis.**—In ordinary cases of acute poliomyelitis the acute stage usually lasts from 1 to 2 weeks. A recrudescence of the acute symptoms is occasionally observed. When death occurs, it is not caused as in many infections, by a general toxemia, but almost always by sudden or gradual palsy of the muscles of respiration, the result of bulbar lesions, or by a complication, especially bronchopneumonia. The time elapsing between the onset of the disease and the fatal issue is in the majority of cases from 3 to 5 days, but it may be only a few hours. Bulbar symptoms rarely develop after the tenth day. The death-rate in various epidemics has ranged from 5 to 25 per cent. It is much lower in sporadic cases. The disease is more fatal in adults than in children. Second attacks are rare, recovery being associated, as a rule, with enduring immunity. In a number of instances acute poliomyelitis has been followed after an interval of several years by progressive muscular atrophy.

As regards the paralysis, the prognosis is doubtful in the extreme. The more rapidly power returns the better the outlook. Paralysis remaining

after the lapse of a few months is usually permanent; nevertheless local treatment should be continued for at least a year or a year and a half, as up to this time some amelioration is still possible. Even the reaction of degeneration does not render the prognosis absolutely hopeless. In some epidemics as many as 1 in 4 or 5 patients have completely recovered. In sporadic cases the percentage of complete recoveries is much less.

**Prophylaxis and Treatment.**—The measures to be taken to prevent the spread of the disease consist of immediate notification of every case, abortive cases included; isolation of the sick in screened rooms for not less than 2 weeks from the onset; the disinfection of the nose and throat discharges and of all articles soiled therewith; the exclusion of children who have been in intimate contact with a patient from public assembly for a period of two weeks from the date of exposure; and during the prevalence of an epidemic the avoidance of opportunities for intimate contact of large numbers of children.

The *treatment* during the acute stage should be that of other acute infections. Absolute rest in bed for several weeks, even in the mildest cases, is essential. Counterirritation interferes with rest and can do no good. Mild diaphoretics and hot packs or hot baths (100° F.) for fifteen minutes, twice a day, seem to be of benefit. Hexamethylenamin (20–30 grains—1.3–2.0 gm. —daily) has been recommended, but as it yields virtually no formaldehyde in the cerebrospinal fluid it is of doubtful value.

Intraspinal and intravenous injections of the serum of convalescent patients have been tried by Netter,[1] Amoss and Chesney,[2] and others, but up to the present time the results have not been conclusive. Rosenow,[3] reports good results from intravenous and intramuscular injections of an immune horse serum prepared by repeated inoculations with a pleomorphic streptococcus isolated from the central nervous system in human poliomyelitis. Of 121 patients treated in the early stages, none died and but one showed slight residual paralysis. Severe pain in poliomyelitis will require the use of acetylsalicylic acid, acetphenetidin, or morphin. Lumbar puncture usually affords much relief. In the event of respiratory failure, oxygen inhalations and artificial respiration should be tried.

The affected limbs should be wrapped in cotton-wool and maintained in such a position that the paralyzed muscles will not become overstretched or their antagonists over active. After the lapse of three or four weeks mechanical treatment should be instituted and systematically practised for a year or a year and a half, if necessary. Massage and passive movements are especially useful in promoting the circulation in the paralyzed members and in counteracting the tendency to contractures. Electricity may also be used with advantage in many cases. The faradic current should first be tried and if to this there is no response recourse should be had to galvanism, the cathode being chosen as the active pole. The weakest current that causes contractions should be used and the applications should be made for ten minutes, four or five times a week. It is doubtful whether any good can be accomplished by using electricity unless the current produces muscular contractions. In the case of young children electric treatment should always be instituted very gradually, otherwise the application may cause so much alarm as to be distinctly harmful; and again, if contractions can be produced only by currents which cause pain it is better to dispense with electricity entirely and depend upon the other measures.

In the course of a few weeks, if the paralysis shows a tendency to recede,

[1] Bull. de l'Acad. de méd., Oct. 12, 1915.
[2] Jour. Exper. Med., April, 1917.
[3] Jour. Amer. Med. Assoc., Aug. 20, 1921.

the patient should be encouraged to make voluntary movements of the affected limbs, the amount of exercise being gradually increased as the power returns. Under no circumstances, however, should attempts at walking without assistance be permitted until the legs are strong enough to bear the weight of the body. Even when the paralyzed muscles show no further tendency toward recovery, much good may be accomplished by the application in suitable cases of light, well-fitting braces, or, if there is excessive contraction of healthy muscles, by tenotomies. In other instances nerve anastomosis, tendon transplantation, tendon-lengthening, or the resection of a joint may serve to increase the usefulness of an affected member.

## EPIDEMIC ENCEPHALITIS

(Lethargic Encephalitis; Noma)

**Definition.**—Epidemic encephalitis is an acute, infectious and mildly contagious disease, characterized anatomically by multiple foci of inflammation in the central nervous system, most marked in the midbrain, and manifested clinically by a diversity of symptoms, but most constantly by fever, lethargy or somnolence and ophthalmoparesis.

**Etiology.**—The disease was epidemic in Europe in 1712 and again in 1890. In the recent outbreak cases were recognized first in Austria in 1917 and then successively in France, England, the United States, and India. It is possible that influenza, which on two occasions, at least, has coexisted with encephalitis, may reduce the resistance of the individual to the virus of the latter, but there is no reason to believe, as some writers have maintained, that the one disease is a variant of the other. Epidemic encephalitis is communicable, but the degree of its contagiousness is relatively low, apparently about that of epidemic poliomyelitis as observed in ordinary times (Flexner). The number of cases in a community at one time has never been very large. The disease occurs at all ages, and affects the two sexes about equally. It prevails especially in cold weather. The inciting agent has not been isolated, but it has been shown to be present in the nasopharyngeal secretions, to be filtrable, and to be infective for rabbits and monkeys. It is probable that mild and abortive cases and healthy carriers play an important part in disseminating the virus.

**Morbid Anatomy.**—The characteristic lesions are confined to the central nervous system and affect chiefly the brain, especially the structures about the aqueduct of Sylvius and lateral ventricles, and the basal ganglia, pons and medulla. The cervical cord may or may not be involved. Macroscopic changes are often absent, but in some cases the meninges are slightly congested and edematous and section of the brain shows scattered pinpoint hemorrhages in both the gray and white matter, and more or less edema. Microscopically, the changes consist of disseminated collections of cells, chiefly small mononuclear forms, about the bloodvessels and in the surrounding nerve tissue of the affected areas, thrombosis of some of the smaller vessels, minute hemorrhagic extravasations, and more or less degeneration of the ganglion cells, although in comparison with epidemic poliomyelitis the parenchymatous alterations are, as a rule, slight.

**Symptoms.**—The symptoms vary considerably according to the site and intensity of the lesions. The most constant features are fever, lethargy or somnolence, and paresis of certain muscles supplied by the cranial nerves,

especially those of the eyes. The onset may be sudden, but it is usually gradual and marked by malaise, nasal or bronchial catarrh, anorexia, nausea, general pains and vertigo. Moderate fever (100°–102° F.), lasting from a few days to two or three weeks, is nearly always present in the more severe forms of the disease, and not rarely in fatal cases death is preceded by very high temperatures. Profuse sweating is occasionally observed. Slight or moderate polymorphonuclear leucocytosis is the rule.

Disturbance of consciousness is the most striking feature in more than 80 per cent. of the cases. It may consist of lethargy, somnolence, stupor, or coma, although the last is somewhat exceptional. Nearly always the patient can be aroused by loud speaking or prodding, but on awakening he appears dazed and uninterested, and when left to himself soon relapses into sleep; and in some cases, although he lies perfectly still, with his eyes closed and his face expressionless, he is not really oblivious to what is going on about him. Other cases present neither sopor nor apathy, and occasionally there is pronounced insomnia. Other mental disturbances, including euphoria, anxiety, delirium, catatonia, and catalepsy, may also occur.

Of the focal manifestations ophthalmoparesis is the most common. It occurs in at least two-thirds of the cases and may precede or follow the lethargy. Diplopia and ptosis are often the only indications, but there may be total external ophthalmoplegia. Pupillary anomalies are relatively infrequent and choked-disc is rare. Occasionally nystagmoid movements are observed. Not uncommonly there is an involvement of the nuclei or roots of certain cranial nerves other than those supplying the eyes, with the occurrence of facial palsy, dysphagia, or dysarthria. Even when the facial nerves are not affected the face often presents a blank, mask-like appearance similar to that seen in paralysis agitans. Paralysis of the limbs is somewhat exceptional, but monoplegias and hemiplegias have been reported. Increased muscle rigidity, or hypertonia, and tremors, which are intensified by voluntary effort, are fairly common in the more severe forms of the disease. Fibrillary twitchings, especially of the abdominal and thoracic muscles, may also occur. Occasionally, the involuntary muscular movements are coarser and take the form of jerks or waves (spinal myoclonus and myokymia multiplex) or even of choreiform contractions (cortical myoclonia). In a few instances convulsions of the Jacksonian type have been observed. The deep reflexes are frequently somewhat exaggerated, but they may be normal or decreased. Babinski's sign is present when the pyramidal tracks are involved.

Sensory disturbances are not usually conspicuous and in many cases are not present at all. Headache is fairly common as an initial symptom and not infrequently it is followed by a persistent sense of soreness in the scalp. Facial neuralgia from involvement of the sensory portion of the fifth nerve, root pains in the trunk and legs, hyperesthesia, hypesthesia, and acute ataxia, usually of the cerebellar type, are occasionally observed. Symptoms referable to irritation of the meninges (stiffness of the neck, Kernig's sign, affected limbs, etc.), if present at all, are, as a rule, poorly developed and ephemeral.

The cerebrospinal fluid is clear, is under normal or slightly increased pressure, and is negative to the Wassermann test and to bacteriologic smears and cultures, but it usually shows a slight or moderate lymphocytosis (20–150 cells), a positive globulin reaction, and a normal or slightly increased sugar content. In rare instances it may contain a small amount of blood.

**Prognosis and Course.**—The mortality of epidemic encephalitis is somewhat difficult to estimate, as doubtless there are many mild and abortive

cases that escape recognition. The fatalities reported average about 20 or 25 per cent. The prognosis is especially grave when there is maniacal delirium instead of lethargy or when myoclonia is a conspicuous feature. Whether the disease ends in death or recovery the course may be short or prolonged, but as a rule fatal cases terminate in a few days or weeks, and favorable cases last many weeks or months. When death occurs it is usually due to paralysis of the respiratory center or to intercurrent pneumonia. In patients who recover the paralytic phenomena usually disappear completely, but in many cases asthenia, insomnia, depression, dizziness, headache, or some degree of mental deficiency persists for long periods or even permanently. Occasionally, choreiform movements, muscular twitchings or tremors are observed as sequels. In some instances the Parkinsonian syndrome, unilateral or bilateral, has persisted and become progressive.

Sequels seem to be especially common in infants and young children, complete recovery having occurred in only 6 of 25 cases reported by Paterson and Spence[1] and in 21 of 62 cases reported by Comby.[2]

**Diagnosis.**—The diagnosis must be made chiefly by exclusion. In any case, however, the association of lethargy or of lethargy and ocular palsies with a normal spinal fluid or a spinal fluid that is negative except for a slight increase in cells or in globulin is strongly suggestive of encephalitis. In *syphilitic meningo-encephalitis* the onset is usually less rapid, fever is absent, and the spinal fluid shows characteristic changes. *Epidemic cerebrospinal meningitis* may usually be distinguished by obtrusive signs of meningeal irritation (rigidity of neck, Kernig's phenomenon, etc.) and by cloudy spinal fluid, with marked pleiocytosis. *Tuberculous meningitis* sometimes occasions difficulty, but in this disease the onset is, as a rule, slow, the palsies are late in appearing, and the spinal fluid contains tubercle bacilli. *Abscess of the brain*, especially of the frontal lobes, may closely simulate epidemic encephalitis, but in the former there is usually evidence of suppuration elsewhere, as in the middle ear or nasal accessory-sinuses and the spinal fluid sometimes presents abnormalities. *Cerebral tumor* may produce a clinical picture very like that of encephalitis, but in the former the symptoms develop slowly, there is no fever, and headache, vomiting, and optic neuritis are much more constant manifestations.

The distinction from the *pontine bulbar spinal type of poliomyelitis* may be exceedingly difficult. In this disease, however, lethargy is exceptional, the paralysis commonly develops more rapidly than in encephalitis, the third nerve is rarely involved, asymmetrical paralysis of the extremities is especially common, the paralysis is maximal almost at once and invariably recedes with the disappearance of the constitutional disturbance, and the fever usually subsides soon after the occurrence of paralysis.

In *botulism* symptoms of bulbar palsy are an outstanding feature and both fever and sopor are usually absent, but the most important point in the differential diagnosis is the occurrence of similar cases among other persons who have partaken of the same food.

**Treatment.**—This is largely empiric. Rest in bed, protection from excitement, an abundance of liquid and semi-liquid food, regulation of the bowels, and careful nursing are first in importance. Lumbar puncture with the removal of from 10 to 20 mils of spinal fluid, at intervals of 3 or 4 days, has been of service in some cases. Hexamethylenamin, in doses of 10 grains (0.6 gm.), three times a day, has been recommended, but it is of doubtful value. In cases with severe headache, restlessness, and insomnia bromids

[1] Lancet, Sept. 3, 1921.
[2] Archiv. de Méd. des Enf., Aug., 1921.

may be used with advantage. During convalescence rest should be continued and supplemented by hydrotherapy and massage.

## TYPHUS FEVER

(Jail Fever; Ship Fever; Tabardillo; Brill's Disease)

**Definition.**—Typhus fever is an acute, specific, infectious disease, occurring chiefly in epidemics, transmitted from person to person through the bite of an infected body louse and characterized by an abrupt onset, marked prostration, severe nervous symptoms, a macular eruption usually becoming petechial, and a continued fever terminating by crisis or rapid lysis in from 12 to 14 days.

**History and Etiology.**—Typhus fever has probably existed from time immemorial, but the first outbreak to be accurately described occurred in Verona in 1506. Extensive epidemics have repeatedly occurred on the Continent of Europe, and England and Ireland suffered severely at intervals until the latter half of the nineteenth century. During and since the recent European war there have been serious outbreaks in Russia and the Balkan States. In the United States there has never been an extensive epidemic, but on several occasions limited outbreaks have occurred in the Atlantic seaboard towns, and in California, the virus having been imported from abroad, and sporadic cases of typhus of a mild type, known as Brill's disease,[1] have occasionally been observed in New York and other cities. Sanitary regulations have done much toward restricting the spread of the disease, and at present it is endemic chiefly in Russia, the Balkans, Northern India, China, Japan, and Mexico. To Gerhard and Pennock[2] belongs the credit of first clearly differentiating typhus fever from typhoid fever.

Epidemics of typhus have almost always developed under insanitary conditions, such as prevail especially in times of war and destitution. Indeed, of the factors concerned in the spread of the disease, the most important are overcrowding and filth. Outbreaks occur chiefly in cold weather, and even in the tropics (Mexico and India) it is the elevated regions that are especially affected. Until recently the disease was believed to be highly contagious and the frequency with which nurses, physicians and other attendants upon the sick were attacked was cited as evidence of its transmission by direct contact or through the medium of fomites. The researches of Nicolle[3] Goldberger and Anderson[4] and Ricketts and Wilder,[5] however, have demonstrated conclusively that the conveyance of the infective agent from person to person is effected solely by the body louse (*Pediculus vestimenti*) and possibly the head louse (*Pediculus capitis*), and that in the absence of such vermin the most intimate contact with the sick is powerless to excite the disease in others. The nature of the causative agent is not definitely known. Plotz[6] has isolated a Gram-positive bacillus (*B. typhi exanthematici*) from the circulating blood, which he claims produces the disease on being inoculated in pure culture in animals and which is agglutinated by the blood serum of

[1] American Jour. Med. Sci., April, 1910; Aug., 1911.
[2] Amer. Jour. Med. Sci., 1837, vols. xix–xx.
[3] Comptes Rendus Acad. de Sci., 1909, cxlix, 157, 486.
[4] Public Health Reports, 1910, xxv; 1912, xxvii.
[5] Jour. Amer. Med. Assoc., Feb. 5, 1910.
[6] Jour. Infect. Dis., 1915, xvii, 1.

patients. More recently, da Rocha-Lima[1] and Wolbach, Todd and Palfrey[2] have regularly found in the blood of typhus patients, as well as in infected lice, a micröorganism which they believe to be the true etiologic factor. This bacterium or protozoön (*Rickettsia prowazeki*[3]) is Gram-negative and pleomorphic, varying in form from minute paired, ovoid bodies to bacillary and filamentous forms measuring several microns in length. The parasite, whatever its nature, undergoes an extrinsic period of incubation in the body of the louse of 4 or 5 days, but whether during this period it goes through a cycle of development has not been determined.

One attack of typhus fever usually confers lasting immunity.

**Morbid Anatomy.**—There are no characteristic macroscopic lesions. The petechial eruption persists after death. The blood is usually dark and fluid. The spleen is, as a rule, large and soft. The liver and kidneys show evidences of cloudy swelling. Hypostatic congestion of the lungs is frequently observed. The distinctive pathology, as Fränkel,[4] Nicol[5] and others have shown, is microscopic, and concerns the smaller bloodvessels, especially those of the central nervous system and skin, but also to some extent those of the heart and other organs. The lesions consist of an accumulation of leucocytes and wandering cells about the arterioles (periarteriolitis) and a proliferation and necrosis of the endothelium, with the subsequent formation of thrombi, usually mural but occasionally occluding, and sometimes in the case of the capillaries, resulting in minute extravasations of blood. In the brain these vascular lesions produce minute areas of necrosis and proliferation corresponding in size to miliary tubercles. Occasionally large vessels, such as the superior mesenteric artery or a main branch of the pulmonary or splenic artery, are involved with thrombosis and infarction.

**Symptoms of Epidemic Typhus Fever.**—*The period of incubation* is usually from 8 to 14 days, but it may be as short as 5 days or as long as 21 days. During this period there are, as a rule, no symptoms. The *invasion* is sudden and marked by chilliness, pain in the head, back and limbs, muscular soreness, prostration and fever. The patient is restless and distressed, the expression is dull, the face is dusky, the conjunctivæ are injected, the skin is pungently hot, and the tongue is furred. Epistaxis is not uncommon. Vomiting may occur, but as a rule the stomach is retentive. The bowels are usually constipated. Insomnia is frequently a troublesome feature and even at this time there may be some delirium, especially at night. As the disease progresses a slight cough with thin mucopurulent expectoration not rarely develops.

The *temperature* rises rapidly, usually attaining its maximum (103° to 105° F.) by the third or fourth day. It remains high with slight morning remissions until about the end of the second week, when it falls by crisis or by a rapid lysis, reaching the normal in two or three days. Occasionally there is a pseudocrisis about the ninth day. When a fatal termination threatens the temperature sometimes rises to an extraordinary height, 108° or even 109° F. The *pulse* and *respiration* are accelerated, usually in accordance with the degree of pyrexia. The *spleen* is sometimes palpable. The *urine* presents the usual febrile characteristics and not infrequently contains albumin. An examination of the *blood* shows in the majority of cases a slight or a moderate leucocytosis of the polymorphonuclear type. The blood

[1] Deutsch. med. Woch., July 3, 1919.

[2] Internat. Jour. Pub. Health, Sept., 1920, No. 2.

[3] Named in honor of these two scientists who gave their lives in studying the etiology of typhus fever.

[4] Münch. med. Woch., 1915, lxii, No. 24.

[5] Ziegler's Beitr., 1919, lxv, No. 1.

serum causes agglutination of certain members of the proteus group (Weil-Felix reaction[1]). This agglutination in a dilution of 1 : 100 or higher within the first six days of illness is said to be highly suggestive of typhus fever, if typhoid can be excluded. Lower dilutions are without diagnostic significance. *The cerebrospinal fluid* is, as a rule, of somewhat high tension and clear or slightly cloudy. In the more severe cases it may be yellow (xanthochromia), and frequently it contains red blood cells (Daniélopolu 3).

*The eruption* of typhus fever consists of distinct macules and an ill-defined mottling of the surface. The characteristic *macules* appear usually on the fourth or fifth day, but they may come out as early as the third or as late

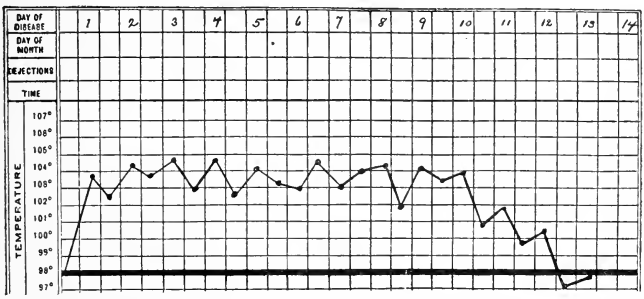


FIG. 11.—Temperature curve of a moderately severe case of typhus fever terminating by rapid lysis.

as the seventh day. They are fairly abundant, as a rule, on the trunk and extremities, but are not commonly seen on the face or palms. They are irregular in outline, very slightly raised, of a rosy-red or purplish hue, and at first disappear when the finger is pressed upon them. In the course of a day or two many of the spots become petechial and no longer fade under pressure. The eruption does not appear in successive crops, as in typhoid fever, but is all out within forty-eight hours. When purely erythematous the macules disappear within a few days but when petechial they may persist until after the crisis. Generally speaking, the severity of the attack is directly proportionate to the number and lividity of the spots. Occasionally the eruption is absent, especially in children. The omission was noted by Murchison only 55 times in 2499 cases at all ages.

In addition to the mulberry rash, as it was termed by Sir William Jenner, there is frequently a *faint, irregular, dusky red efflorescence*, which appears to be more deeply seated than the macules. This "subcuticular mottling" not infrequently comes out as early as the second or third day.

With the appearance of the exanthem the *toxemia* increases in severity. The prostration now becomes extreme. Delirium, usually low and muttering, but sometimes noisy and violent, supervenes and is followed by increasing stupor, or, in cases about to end fatally, by actual coma. The insomnia of the early stage often continues despite the stupor. The respiration becomes hurried, the pulse frequent and compressible, and the systolic sound of the heart feeble. The expression grows more and more vacant, the complexion takes on a dingy appearance, and the pupils contract to mere points. The

[1] Wien. klin. Woch., 1916, xxix, Nos. 2 and 31; 1917, xxx, No. 48.

[2] *Le Typhus Exanthématique;* D. Daniélopolus, Bucharest, 1919.

tongue becomes dry and brown, and sordes collect on the teeth. Constipation is the rule, but diarrhea not rarely sets in late in the disease. In grave cases twitching of the muscles, subsultus tendinum, carphologia (picking at the bed clothes or at imaginary objects), and loss of control over the bladder and rectum often accompany the stupor or delirium. Coma vigil, a state in which the patient, although in deep stupor, lies with his eyes wide open and fixed, is now and then observed. In many cases of typhus the body exhales a peculiar odor, which has been likened to that of rotten straw.

In cases terminating favorably defervescence occurs at the end of the second week. It may be abrupt, but in the majority of cases it occupies two or three days. With the fall in the temperature all of the symptoms undergo marked amelioration. *Convalescence* is generally rapid but it may be retarded by complications. When death occurs, it is usually through coma or syncope and between the tenth and fourteenth days. Occasionally a fatal termination is preceded by a sudden rise of temperature or by convulsions.

**Variations.**—In nearly every epidemic there are many mild cases in which the temperature does not exceed 102°, the eruption is scanty and persistently erythematous, the severe nervous symptoms are wholly wanting, and the disease runs its course in about ten days. The sporadic form of typhus (*Brill's disease*) is almost invariably of a mild type. On the other hand, there are cases (*typhus siderans*) in which the symptoms set in with great violence and the patient, overwhelmed by the intensity of the poison, succumbs within a few days. Between these extremes, there is every conceivable grade of severity.

**Complications.**—Bronchitis, hypostatic congestion of the lungs and bronchopneumonia are by no means uncommon. Lobar pneumonia, nephritis and endocarditis are rare. Parotitis, otitis media and phlebitis have been frequent in some epidemics. Bedsores, boils, subcutaneous abscesses, suppuration of the joints, erysipelas, cancrum oris, and gangrene of the digits or nose are occasional complications. Jaundice may occur. Peripheral neuritis has been observed.

**Diagnosis.**—At times, particularly at the commencement of an epidemic, and in mild sporadic cases, it may be difficult to distinguish typhus fever from typhoid fever and cerebrospinal fever. As the rash alone is not distinctive, it is necessary to consider carefully all the features of the case. In *typhoid fever* there are almost always prodromal symptoms, the onset is, as a rule, insidious, the temperature curve both rises and falls gradually, the pulse is less rapid than in typhus, the eruption appears later, comes out in successive crops and rarely becomes petechial, subcuticular mottling is scarcely ever observed, the conjunctivæ are not often injected nor are the pupils contracted, abdominal symptoms are usually marked, and the blood gives a positive Widal reaction and frequently shows the Bacillus typhosus on culture. In *cerebrospinal fever* the temperature is very irregular, vomiting is common, the petechial eruption is inconstant, herpes occurs with considerable frequency, there is a marked tendency to rigidity of the neck, to retraction of the head and to paralysis of the cranial nerves, Kernig's sign is rarely absent, and fluid obtained by spinal puncture is rich in cells and usually contains the specific microörganism.

The resemblance of typhus fever to *Rocky Mountain spotted fever* is very close and in localities in which the latter prevails the differential diagnosis might present insurmountable difficulties. In Rocky Mountain spotted fever the fever is usually more gradual in onset and termination and of longer duration than in typhus, pain is especially severe in the larger joints,

and the eruption almost always appears first about the ankles and wrists and then rapidly spreads to all parts of the body.

**Prognosis.**—The mortality varies in different epidemics. It may exceed 50 per cent., but the average is probably between 10 and 20 per cent. The death-rate of the sporadic form (Brill's disease) is less than 1 per cent. In old persons and individuals exhausted by privation, fatigue, or preexisting disease the outlook in epidemic typhus is especially grave.

**Prophylaxis and Treatment.**—*Prophylaxis* consists in the destruction of lice on the body and clothing of the patient, of contacts and of persons who have come from infected communities. The patient himself must be isolated in a room that is free from vermin, and physicians, nurses, and other attendants on the sick should wear vermin-proof clothing. A powder consisting of naphthalen, 96 per cent.; creosote, 2 per cent.; and magnesium silicate, 2 per cent. has been found of some value of keeping lice out of clothing (Kinloch), but clothing already infested can be sterilized effectively only by biling or by subjection to superheated steam. In Serbia, Strong found the coal oil bath a reliable means of ridding the body of lice and their eggs.

The *treatment* of typhus is that of any acute infective disease. Absolute rest in bed, an abundance of fresh air, and careful nursing are especially important. As the process is an exceptionally depressing one, the strength should be maintained by sufficient nourishment of a readily digestible character, and often by alcohol. Drinking water should be offered freely and often. A daily cleansing bath and the use several times a day of a boric-acid mouth wash are indicated. Cardiac stimulants, such as caffein, digitalis, camphor, etc., are commonly required. Daniélopolu[1] speaks very favorably of frequent intravenous injections of salt solution (0.65 per cent.). The fever is best controlled by hydrotherapy. Headache and other nervous symptoms may sometimes be relieved by applications of cold to the head, but if severe, they may require the use of bromids or even of morphin.

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## ROCKY MOUNTAIN SPOTTED FEVER

(Rocky Mountain Fever)

**Definition.**—Rocky Mountain spotted fever is an acute infectious disease prevailing in certain localities in the Rocky Mountain and Pacific Coast States, and characterized by chills, moderately high fever, neuromuscular pains and an eruption which is at first macular and then petechial.

**Etiology.**—The disease prevails especially in the Bitter Root Valley of Montana and in the Snake River Valley of Idaho, but it occurs also in certain parts of Washington, Oregon, California, Wyoming, Nevada, and Utah. It usually appears in the spring and summer months and is observed most frequently among persons who work in fields and forests. The disease is not directly contagious, and a single case to a house is the rule. The two sexes are equally susceptible, but men are more frequently attacked, owing to their occupations, which expose them to infection.

The cause of Rocky Mountain fever is not known, but the researches of Ricketts have shown that whatever its nature it is conveyed to man by the bite of a tick, *Dermacentor occidentalis* (*D. andersoni*), which lives on domesticated animals and which becomes infected by feeding on ground squirrels, chipmonks, ground hogs, and other small wild animals of the endemic area.

[1] *Loc. cit.*

Experimentally the infection is transmissible to guinea pigs and monkeys by inoculation of the blood of patients. Recently, the inciting agent of Rocky mountain fever has been held to be a species of Rickettsia (*Dermacentroxenus rickettsi*), a minute organism similar to that which da Rocha-Lima, Wolbach, Schulz[1] and others believe to be the specific organism of typhus fever.

**Morbid Anatomy.**—The most constant macroscopic findings are hemorrhagic extravasations into the skin, chiefly in the form of petechiæ, enlargement of the spleen, congestion and cloudy swelling of the kidneys, and fatty infiltration of the liver. According to Wolbach,[2] the specific lesions are microscopic and involve the minute bloodvessels, especially those of the skin and genitalia. The changes consist of an accumulation of leucocytes about the vessel and an endangeitis, characterized by proliferation and necrosis of the endothelium and thrombosis.

**Symptoms.**—After a period of incubation of from 3 to 10 days the disease sets in suddenly with a chill, headache, severe pains in the muscles and joints, and fever. The temperature rises rapidly, with morning remissions, until it reaches 103°, 104° or even 105° F. in the course of a few days. In the milder cases defervescences by lysis begins about the tenth or twelfth day and the temperature reaches normal within the third week. The face is flushed, the conjunctivæ are injected, the pulse is frequent and often out of proportion to the temperature, the bowels are constipated, the spleen is enlarged and tender, and the urine is scanty and slightly albuminous. Jaundice is not uncommon. In severe cases the patient becomes delirious and passes into a typhoid state. A characteristic feature is the eruption, which appears on the second to the fifth day about the wrists and ankles, and then spreads over the body, becoming especially marked on the back. It is at first bright red and macular, but it rapidly becomes darker and after a few days it is usually definitely petechial. With defervescence the eruption gradually fades and during convalescence desquamation occurs. Gangrene of the skin in certain parts, especially of the scrotum or prepuce, and edematous swellings are sometimes observed. The leucocytes of the blood are usually increased (10,000–15,000).

**Diagnosis.**—In the localities in which spotted fever prevails the diagnosis presents few difficulties. The resemblance to *typhus fever*, however, is close. The eruptions are similar, but that of typhus usually appears first on the trunk and then spreads to the limbs. The fever in typhus is more abrupt in both its onset and termination and the course of the disease is, as a rule, shorter. In typhus the transmitting agent is the body louse, in spotted fever it is a tick. *Typhoid fever* may be distinguished by the more gradual onset, the relative infrequent pulse, positive Widal test and blood cultures, and the character and distribution of the eruption.

**Prognosis.**—The mortality varies remarkably in different localities. In Montana it is between 70 and 90 per cent., while in Idaho it is less than 5 per cent. The duration of the disease varies from a week or ten days in fatal cases to 3 or 4 weeks in those that end favorably. Pronounced nervous symptoms are of ill omen.

**Treatment.**—Protection against the bite of ticks is the important prophylactic measure. Sheep-grazing has been recommended as a means of tick eradication (Frick[3]), the insects being destroyed probably by tangling themselves in the wool of the sheep. The treatment is that of typhus fever (see p. 277).

[1] Amer. Jour. Med. Sci., Jan., 1921.
[2] Jour. Med. Research, 1918, No. 3, 37.
[3] Pub. Health Rep., Jan. 15, 1915.

## TRENCH FEVER

**Definition.**—Trench fever is a specific infectious disease, occurring chiefly in soldiers occupying trenches on the battle line, and characterized by a sudden onset, generalized pains, hyperesthesia of the skin, leucocytosis, and moderate fever, which continues for 3 or 4 days and then intermits, to be followed by one or several relapses.

**Etiology.**—The disease, which was especially prevalent in the British army in France and Saloniki during the recent European war, was first described by Graham[1] in 1915. The inciting agent is not known, but according to the Medical Research Committee of the American Red Cross[2] it is a resistant filterable virus and is present in the blood plasma and sometimes in the urine and sputum. The marked tendency of the fever to relapse at definite intervals is suggestive of a spirochetal origin. According to Wolbach[3] a Rickettsia organism similar to that occurring in typhus fever has been found in the tissues in trench fever. Apparently, the disease is transmitted by the body louse, either by its bite alone or by its excrement, which is infective when rubbed into an abraded skin. As lice do not become infective until at least a week after feeding on a trench fever patient, it is likely that the organism undergoes a developmental cycle within the insect.

**Symptoms.**—The period of incubation is said to vary from 14 to 24 days. The onset is sudden and marked by chilliness, dizziness, headache, pains in the back and limbs, and fever. Accompanying the pains, there is often pronounced hyperesthesia of the skin. The tongue is, as a rule, only lightly coated and derangements of the digestive tract are uncommon. Nystagmus on lateral motion of the eyes is observed in a large proportion of cases. The temperature rises rapidly to 102°, or 103°, or even 104° F., continues high, until the third or fourth day and then falls to normal, to be followed after an interval of a day or two by a second rise lasting two or three days. After the second febrile paroxysm recovery may rapidly ensue or there may be a single relapse or several relapses at fairly regular intervals, each succeeding relapse being of shorter duration than the one preceding it. In about one-half of the cases an evanescent, rosy, macular eruption appears on the trunk, in successive crops, both in the primary attack and in the relapses. The spleen is frequently palpable and moderate leucocytosis is the rule. There are no signs of catarrh of the respiratory tract, herpes is rare, and the urine shows merely febrile changes. In the intervals between the febrile paroxysms the patient feels fairly well, although he frequently complains of more or less pains in the shins. Complications are rare and recovery always ensues. The duration of the disease when there is not more than one relapse (*short type*) is about 2 weeks. With the occurrence of several relapses (*long type*) the duration may be extended to 4, 5, or even 6 weeks. Occasionally trench fever is followed by a state of ill health, lasting several months.

**Diagnosis.**—From *influenza*, the disease may be distinguished by the absence of catarrhal symptoms and the presence of leucocytosis, the peculiar shin pains, the relapsing type of fever and, frequently, cutaneous hyperesthesia and nystagmus. *Relapsing fever* may be excluded by the short duration of the febrile paroxysms and the absence from the blood of the characteristic spirochetes; *dengue*, by the absence of leucopenia, joint pains and pronounced mental and physical depression; and *rat-bite fever*, by the

[1] Lancet, 1915, ii, 703.
[2] Report of Commission, 1918.
[3] Jour. Amer. Med. Assoc., May 28, 1921.

history and the absence of enlargement of the regional lymph-nodes and of the bluish-red blotchy eruption.

**Prophylaxis and Treatment.**—Prophylaxis consists in the destruction of body lice and the disinfection of the urine and sputum. The treatment is purely symptomatic.

## YELLOW FEVER

**Definition.**—Yellow fever is an acute, infectious but non-contagious disease, endemic in the maritime districts of certain tropical countries, contracted through the bite of an infected mosquito, and characterized by one or two febrile paroxysms, jaundice, albuminuria, and a marked tendency to hemorrhages, especially from the stomach.

**Etiology.**—Modern research has demonstrated that yellow fever is not contagious in the ordinary sense of the term but is transmitted through the intermediary of the mosquito *Stegomyia calopus* (*S. fasciata*).

The doctrine of the transmission of yellow fever by the mosquito was first suggested by Nott in 1848,[1] was strongly advocated and advanced by Finlay, of Havana, in 1881,[2] and was firmly established through the notable experiments of Reed, Carroll, and Lazear in 1900–01,[3] in one of which Lazear sickened and died.

The female insect is infected by biting a yellow fever patient in the first three days of the disease and can convey the infection only after the lapse of at least twelve days. The ingestion of fresh blood appears to be indispensable to the development of her eggs. Aside from the bite of the infected mosquito, the disease can be transmitted only by the subcutaneous injection of blood taken from a patient during the first three days of his illness. Contact with the patient, his personal effects, or his excretions is devoid of danger.

The stegomyia is a domestic mosquito propagating by preference in cisterns, rain-gutters, ditches and pools in the immediate neighborhood of houses. It feeds chiefly at twilight, hence the inhabitants of infected districts can go about in bright daylight in comparative safety. As it is rarely encountered at an elevation of more than 1000 feet, persons dwelling in high altitudes enjoy more or less protection. It thrives best in a moist climate with a temperature ranging between 76° F. and 86° F. It can be transported by persons or ships into regions where it does not naturally exist and will live and even multiply if the atmospheric conditions are not too unfavorable. At temperatures below 55° F. the insect becomes inactive and ceases to bite, and therefore outbreaks of yellow fever are invariably interrupted or terminated by frost.

At present the chief endemic centers for yellow fever are Central America, Merida in Yucatan, certain towns in Venezuela, along the coast of Brazil and along the west coast of Africa. In this country the Southern states, until the beginning of the present century, were repeatedly invaded and on several occasions (1693, 1763, 1793, 1802) the disease appeared in the large cities of the Atlantic coast from Charleston to Boston. Philadelphia lost 10 per cent. of its population in the epidemic of 1793. The last extensive outbreak in the United States occurred in the Southern States in 1878. In view of the fact that measures directed solely against the mosquito have been so successful

[1] New Orleans Med. and Surg. Jour., 1848, vol. iv.

[2] Anal. de la Acad. de Ciencias Med. de la Habana, xxvii, 1890–01.

[3] Proceed. of Amer. Public Health Assoc., 28th Annual Meeting, Indianapolis, Oct. 1900 and Jour. of Amer. Med. Assoc., Feb. 16, 1901.

in controlling the disease in Havana, Vera Cruz, and Rio Janeiro, three important seed-beds of infection, it seems certain that before the lapse of many years this frightful scourge of humanity will have become entirely extinct.

Although the manner in which yellow fever is transmitted is now definitely known, there is still some dispute in regard to the inciting agent of the disease. Whatever its nature, the organism must be extremely small, since it passes readily through filters capable of holding back ordinary bacteria. All experiments go to show that it does not usually exist in the blood after the third day of the attack (unless relapse occurs) and that it is extremely sensitive, being destroyed in a few minutes at a temperature of 131° F. (55° C.).

Recently, Noguchi[1] isolated from the blood of yellow fever patients a minute, delicate, spiral organism (spirochæta), which he claims produces all the characteristic features of the disease on being inoculated into animals. This organism, which has been named *Leptospira icteroides* ("slim spiral, the jaundice maker"), does not grow on ordinary bacterial culture mediums and can be detected only by means of the dark field microscope. Morphologically, it closely resembles Spirochæta icterohæmorrhagiæ of infectious jaundice but can be distinguished by immunity reactions.

Yellow fever occurs at all ages. In young children, however, it is often so benign as to be overlooked. The colored race is less susceptible than the white. Strangers in infected districts furnish proportionately more victims than the natives, since most of the latter have had the disease in infancy or early childhood, and one attack usually confers immunity for life.

**Morbid Anatomy.**—Rigor mortis is marked. The tissues are stained yellow. Hemorrhages are frequently found in the skin, in the mucous membranes, beneath the serous membranes, and in the substance of the various organs. The stomach usually contains dark liquid blood ("black vomit"), and its mucous membrane, as well as that of the upper bowel, is swollen, congested and blood stained. The liver is firm and yellowish-brown in color, or mottled in appearance, patches of yellow and reddish-brown alternating, as in an autumn leaf. Microscopically, the hepatic cells are swollen, granular, and fatty. The kidneys present the lesions of acute diffuse nephritis. The spleen is congested but not often enlarged. The heart is flaccid and occasionally fatty. The lungs show hypostatic congestion with hemorrhages.

The poison of yellow fever seems to act with greatest severity upon the liver cells and the endothelium of the capillaries. There is no evidence of hemolysis. The jaundice is apparently due to the compression of the minute bile-ducts by the swollen hepatic cells and the general hemorrhagic tendency to the increased permeability of the vessels. The special frequency of hematemesis is attributable to the marked stasis of blood in the stomach resulting from the pressure of the swollen liver cells upon the portal capillaries.

**Symptoms.**—The *incubation period* lasts from 2 to 6 days. The onset is sudden and marked by chilliness, frontal headache, pains in the back and limbs, and more or less prostration. The temperature rises rapidly to 102° or 103°, or in grave cases to 105°, the face is flushed, the eyes are injected, glistening and watery, and the skin is red and dry. The tongue is lightly furred in the middle and abnormally red at the tip and edges. The gums are swollen and hyperemic. Epistaxis is not uncommon. The stomach is irritable from the onset, sometimes rejecting everything that is swallowed. The epigastrum is tender and deep pressure over this region occasions much distress and a tendency to vomit. The bowels are inactive. Jaundice is rarely marked before the third day, although a slight icteroid tinge of the

[1] Jour. Exp. Med., 1919, xxix; 1919, xxx; 1920, xxxi.

conjunctivæ is sometimes apparent by the close of the first day. The urine is scanty and often contains a trace of albumin as early as the second or third day. The patient is apprehensive and restless, but not usually delirious. The pulse rate is low in proportion to the temperature, seldom exceeding 110, and still more important, it shows a marked tendency to decline while the temperature is still stationary or even is rising (Faget's sign). Occasionally, the pulse-rate drops to 60 or even to 50 a minute.

In many cases on the second or third day the temperature falls several degrees and the patient experiences great relief (stage of calm). Indeed, in mild attacks the defervescence may continue through a process of lysis lasting three or four days and be succeeded by rapid convalescence. In well marked cases, however, the remission is of short duration. The tem-

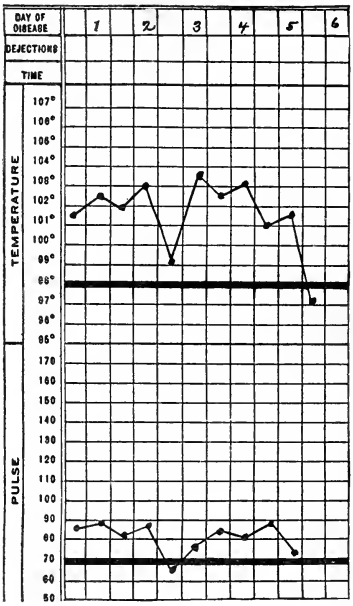


FIG. 12.—Temperature curve of a mild case of yellow fever, showing a remission on the third day.

perature rises again to its original height or higher, while the pulse-rate steadily declines, a purplish discoloration of the skin displaces the red blush of the early stage, the jaundice deepens, and the vomiting returns. At this time the vomited matters, hitherto colorless or yellowish gray, frequently contain minute dark streaks resembling the legs or wings of flies or may consist almost entirely of dark semi-liquid blood ("black vomit"). This fluid often gushes out of the mouth with considerable force and nearly always produces a sensation of burning in the throat and epigastrium. At the same time the stools may assume a tarry appearance from the presence of

altered blood, and bleeding may also occur from the tumid gums and from other mucous membranes, as well as into the skin, producing petechiæ or even large ecchymotic patches. The urine becomes highly albuminous, more and more scanty, and finally may be almost or quite suppressed. In addition to albumin, it contains hyaline and granular casts, bile-pigment, and more or less free blood. The diazo reaction is not present (Guiteras).

On the approach of a fatal termination, the patient becomes apathetic, the skin acquires a cold clammy feel, the pulse fails, the respirations become shallow and infrequent, the body exhales a peculiar cadaveric odor, and delirium or coma supervenes. Occasionally death occurs in convulsions.

The blood presents no signs of corpuscular disintegration (Sternberg Finlay, Schmidt, and Marks). In the early stage, the number of red cells is often normal or even increased and the percentage of hemoglobin is high, often 100, and rarely below 90 (Guiteras). There is usually no leucocytosis.

**Duration.**—In the fatal cases death takes place most frequently between the fourth and the sixth days, although it may occur as early as the third or as late as the tenth day. In cases ending in recovery the average duration is about 8 or 9 days. Relapse is rare but may occur.

**Variations.**—Many variations are observed in the course of the disease. In all epidemics there are *mild cases*, in which the only symptoms are headache, malaise, and slight fever. Even the yellow tint of the eye-balls may be absent. On the other hand, there is a *malignant type* in which the patient is suddenly striken down while walking or at work and dies within 48 hours in collapse. Sometimes on the second or third day of the attack the temperature suddenly drops to subnormal, black vomit and suppression of urine supervene, and death speedily ensues without the occurrence of secondary fever. In other cases the course of the disease is considerably prolonged by the persistence of the reactionary fever or the development of a typhoid condition. Occasionally the invasion is marked by maniacal delirium.

**Sequelæ.**—Yellow fever is followed by but few sequelæ. Septic processes, such as parotitis, subcutaneous abscesses, and phlebitis, are occasionally observed. After very severe attacks gastric irritability, diarrhea, or general debility sometimes persists for several months.

**Diagnosis.**—The important diagnostic features of the early stage are the sudden onset, pain in the head, back and limbs, general capillary turgescence, ocular jaundice, irritability of the stomach, marked epigastric tenderness, Faget's sign, early albuminuria, high count of red blood-cells, and high percentage of hemoglobin.

The diseases with which yellow fever is most likely to be confused are malaria, dengue, relapsing fever, acute yellow atrophy of the liver and infectious jaundice (Weil's disease).

*Malaria* may be distinguished by the presence in the blood of the specific sporozoa, the low percentage of hemoglobin, the splenic enlargement, and by the absence of early ocular jaundice, early albuminuria, Faget's sign, bleeding gums and black vomit.

In *dengue* jaundice and albuminuria are rare and probably never occur so early as the second or third day, the pulse is accelerated in proportion to the fever, pronounced epigastric tenderness is rarely observed, the joints especially are painful and sometimes swollen, eruptions are much more common and hemorrhages are much less common than in yellow fever, and there is an early and pronounced leucopenia.

In *relapsing fever* the large characteristic spirochete is found in the blood during the febrile paroxysms, the spleen is enlarged, leucocytosis is the rule,

jaundice is usually absent, hemorrhages are uncommon, there is no relative bradycardia, and albuminuria rarely appears as early as the second day.

*Acute yellow atrophy* may be recognized by the gradual onset, the progressive diminution of the liver dulness, the presence of leucin and tyrosin in the urine, and in many cases by the absence of fever.

In *infectious jaundice* the fever is irregular, the liver is enlarged, leucocytosis is the rule, relative bradycardia is uncommon, and there is less tendency to hemorrhages than in yellow fever.

**Prognosis.**—The mortality of yellow fever varies in different epidemics. In some outbreaks more than three-fourths of those attacked have died, while in others the death-rate has been less than 10 per cent. The average mortality is about 20 per cent. Old age, alcoholism, excesses, insufficient food, and overwork all increase the danger. In young children the disease is often so benign as to escape recognition. Negroes are less severely attacked, as a rule, than whites. In individual cases moderate febrile disturbance (100°–102° F.) at the outset, a moist skin, a retentive stomach, a free secretion of urine are favorable signs; while a high temperature (104°–105° F.) a sluggish capillary circulation, persistent vomiting, excessive restlessness, apprehensiveness or delirium, deep jaundice, a scanty flow of urine with increasing albuminuria, and a tendency to bleed from mucous membranes are of grave significance. Black vomit while extremely dangerous, is not necessarily fatal.

**Prophylaxis.**—The spread of yellow fever can be most effectually controlled by the institution of measures tending (1) to reduce the number of mosquitoes to a minimum, (2) to protect the sick from the bites of mosquitoes, and (3) to lessen the chances of non-immunes being bitten by infected mosquitoes. All unnecessary accumulations of still water should be removed. Collections of standing water that are absolutely necessary should be rendered mosquito-proof by converings of fine wire gauze (18 meshes to the inch) or, if this is impracticable, treated once a week with fuel oil or kerosene. Mosquitoes in rooms should be destroyed by thorough fumigation, preferably with sulphur. Persons known to have yellow fever or even suspected of having the disease should be isolated, confined to mosquito-proof rooms, and treated in mosquito-proof beds. Non-immunes should live in mosquito-proof houses, preferably in high localities, outside of the infected region, and, should avoid the latter, if possible, between 3 P.M. and 9 A.M. Persons coming on ships from infected ports should be quarantined for at least five days. Noguchi[1] has used a vaccine consisting of the killed culture of Leptospira icteroides in prophylaxis with apparently favorable results. The duration of the immunity is said to be at least six months.

**Treatment.**—Noguchi[2] reports that when a serum prepared by him in the horse is used on or before the third day in doses of ½ to 1 mil the mortality in yellow fever is much reduced. Of 170 patients who received the serum only 13 died (13.6 per cent.), whereas of 783 patients who received no serum, 442 died (56.4 per cent.). After the fourth day the serum is said to have no appreciable effect. Other treatment of yellow fever is entirely symptomatic. Absolute rest and quiet, a sick-room well ventilated but free from drafts, and careful nursing are essential. Mild attacks are readily made serious by imprudent physical exertion. Many clinicians of large experience advocate the withholding of all food during the first two or three days, prefering to give instead carbonated alkaline drinks at frequent intervals. Natural Vichy water, which is rich in sodium bicarbonate, appears

[1] Jour. Amer. Med. Assoc., Jan. 8, 1921.
[2] Jour. Amer. Med. Assoc., July 16, 1921.

to be particularly useful. It may be taken iced or cool according to the taste of the patient. Even after the stomach has become retentive only the blandest articles of food should be allowed and these should be given in small quantities. Barley-water, toast-water, milk with lime-water, peptonized milk, koumiss, chicken broth and iced champagne are appropriate. If the patient is seen within the first twenty-four hours of his illness a hot mustard foot-bath may be given with advantage. If there is a tendency to constipation calomel may be administered followed by a Seidlitz powder. Persistent vomiting should be combated by the application of sinapisms or an ice-bag to the epigastrium and by the administration of gastric sedatives, such as cracked ice, lime-water, bismuth subcarbonate, cocain and hydrocyanic acid. Morphin, as a rule, should be avoided. Systematic cold sponging keeps down the temperature, lessens nervous irritability, and favors diuresis. High temperature is best controlled by the cool bath. Suppression of urine will call for dry cupping over the loins, alkaline diuretics, hot packs and rectal injections of hot saline solution (105°–110° F.). If there are evidences of cardiac weakness such stimulants as digitalis and strychnin should be used. Threatened collapse will require subcutaneous injections of camphor and enteroclysis or hypodermoclysis with saline solution. Remedies have little effect upon black vomit. Solution of epinephrin, tincture of ferric chlorid and oil of turpentine have been recommended. The patient should not be allowed to leave his bed until at least a week has elapsed from the termination of the secondary fever. The return to solid food should be effected very gradually.

## DENGUE

(Dandy Fever; Breakbone Fever)

**Definition.**—Dengue is an acute, infectious, non-contagious, epidemic disease, apparently contracted by the bite of an infected mosquito, characterized by severe articular pains, two febrile paroxysms, leucopenia, and a somewhat variable rash, and terminating favorably usually in from a week to ten days.

The term dengue is of somewhat uncertain origin. It seems to have been applied to the disease first by the inhabitants of St. Thomas on account of the stiff, awkward gait of those affected with it, and is probably a corruption of the Spanish equivalent of dandy—denguero.

The disease was first recognized by Brylon, in Java, in 1779 and by Rush, in Philadelphia, in 1780. Epidemics have frequently occurred in India, the Sunda Islands, the Philippine Islands, Australia, Egypt, Syria, Spain, the West Indies and the Gulf States of the United States. On a few occasions dengue has appeared in Philadelphia, New York and Boston.

**Etiology.**—Outside of the tropics dengue prevails chiefly in summer, epidemics being almost invariably arrested by the occurrence of frost. Susceptibility to infection is remarkably general and when the disease appears in a community not rarely from one-half to three-fourths of the entire population are stricken with it. Persons of all races, of all ages, and of both sexes are indiscriminately attacked.

The studies of Graham,[1] of Bancroft,[2] of Ashburn and Craig,[3] and of

[1] Jour. Trop. Med., 1903, 5, 209.
[2] Australasian Med. Gaz., 1906, 25, 17.
[3] Philippine Jour. of Sci., 1907, 2, 71.

Cleland, Bradley and McDonald[1] have shown conclusively that dengue is not contagious, but infectious, in the same manner as yellow fever and malaria, and that it is transmitted by the *Culex fatigans* mosquito, and probably also by *Stegomyia*. The exciting cause of the disease is not known, but it is undoubtedly a filtrable virus, for Ashburn and Craig have shown that intravenous injections of the blood of dengue patients, even after it has passed through a diatomaceous filter, are capable of producing the disease in susceptible persons. The similarity of dengue to yellow fever, both in its manner of transmission and in its clinical features, is strongly in favor of its spirochetal nature.

**Symptoms.**—The *period* of *incubation* is from two to six days. The onset is usually sudden and marked by chilliness and malaise. Pains in the head, eyeballs, back and joints, often of great severity, rapidly ensue. Both small and large joints are affected, and sometimes the pain is aggravated by manipulating and is accompanied by swelling of the periarticular tissues, as in rheumatism.

The temperature rises rapidly, often reaching its maximum, 102°, 103° or even 105° F., on the first day, and on the third or fourth day it falls to normal. Defervescence at once brings relief from the pains, although it is frequently accompanied by profuse sweating and more or less exhaustion. In a large proportion of cases the remission is followed in from twenty-four to forty-eight hours by another paroxysm of fever and pain, which, however, is always milder and shorter than the first. An eruption usually appears on the fourth to the sixth day, but is not uniform in character, being sometimes like that of scarlet fever, sometimes like that of measles, and occasionally like urticaria. It fades rapidly and is commonly followed by a fine, branny desquamation. In addition to this true exanthem, a fugitive erythematous efflorescence, analogous to the prodromal rashes of variola, typhus fever, etc., is sometimes observed at the beginning of the disease.

In typical cases the eyes are injected and watery, the face is flushed, the tongue is heavily furred, the pulse is frequent in proportion to the temperature, and the urine is febrile, although rarely albuminous. The stomach is, as a rule, retentive, but in some cases nausea and vomiting are prominent features. Enlargement of the lymph-nodes is not uncommon and occasionally hemorrhages occur from the mucous membranes. Aside from insomnia, nervous symptoms are unusual, except in young children in whom delirium is comparatively frequent. Leucopenia (5000–3000) is an almost constant phenomenon, the decrease in the cells affecting especially the polymorphonuclear forms.

The average *duration* of the disease is from a week to ten days. Relapse is not rare. One attack usually, but not invariably, protects from another. In the vast majority of cases there are no complications. Convalescence, however, is sometimes slow and marked by neuralgic pains, adynamia, and depression of spirits. Death from the disease is rare.

**Diagnosis.**—The diseases with which dengue is most likely to be confused are influenza, acute rheumatism, malaria, and yellow fever. In *influenza* catarrhal symptoms are usually prominent, there is no remission, joint pains are absent, and the only eruption is herpes. Influenza, moreover, prevails especially in cold weather. *Rheumatism* is not epidemic, runs a more protracted course than dengue, lacks an eruption, is attended with leucocytosis, and is productive of serious cardiac complications. *Malaria* is distinguished by the specific blood parasites and the enlarged spleen. The differential diagnosis between dengue and *yellow fever* is considered on page 283.

[1] Med. Jour., Australia, 1916, 4, 204.

**Prophylaxis and Treatment.**—*Prophylaxis* should be along the same lines that have proved successful in yellow fever and malaria. The *treatment* is purely symptomatic. Rest in bed, a plentiful supply of fresh air, and a light, nutritious diet are important. At the beginning a free movement of the bowels should be secured by fractional doses of calomel, followed by a saline. Relief from the pains is usually afforded by acetphenetidin or a salicylate, but occasionally it may be necessary to use morphin. Tonics are often required during convalescence.

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## RABIES

(Hydrophobia; Lyssa)

**Definition.**—Rabies is a specific infectious disease of certain animals, especially dogs and wolves, communicated to man by direct inoculation, and characterized in its early stages by extreme nervous irritability and violent convulsive attacks, involving particularly the muscles of deglutition and respiration, and in its later stages by ascending paralysis, exhaustion and coma.

**Etiology.**—The disease is widespread, but is more prevalent in Russia, Hungary, France, and China than elsewhere. England at present is virtually free of it owing to strict enforcement of muzzling regulations. Outbreaks are occasionally observed in the United States. The largest number of cases occur during the spring and summer months.

Man acquires the disease solely through the bite of an animal affected with rabies, usually a dog, but sometimes a wolf, fox, cat, cow, goat or horse. The bite of wolves is apparently more virulent than that of dogs. Only from 10 to 20 per cent. of persons bitten by rabid dogs become infected. Bites about the face and hands are much more dangerous than bites through clothing. The virus is probably a microörganism but its exact nature is unknown. It is present in the saliva, in the cerebrospinal fluid, and in every part of the nervous system, but apparently not in the blood or viscera. It is readily destroyed by heat and drying.

In the dog the disease is marked by increasing restlessness, a tendency to hide or to stray away from home, a peculiar muffled, plaintive bark, outbreaks of furious excitement, with a disposition to swallow foreign bodies of all kinds and to attack everything in his way or even imaginary objects, and, finally, a rapidly increasing paralysis, the hind legs or the lower jaw, as a rule, being first affected. Less frequently, after a short period of restlessness and depression, paralysis supervenes at once without any intermediary stage of excitement (dumb rabies). Contrary to popular belief the rabid dog has no fear of water.

**Pathology.**—The only characteristic lesions are microscopic and these are found in the nervous system. Especially important in making possible an early histological diagnosis in suspected animals are the peculiar bodies discovered by Negri[1] in the cytoplasm of the large nerve cells. These bodies are sharply defined, round or oval hyaline structures, presenting, when properly stained, one or more chromatin bodies. They are most abundant, as a rule, in the multipolar cells of the hippocampus major (Ammon's horn), but they may also be found in the cells of the cerebral cortex, cerebellar cortex, and spinal ganglia. That Negri bodies are specific is well established,

[1] Boll. d. Soc. med.-chir. di Pavia, 1903.

and that they are protozoan parasites, as Negri himself believed, is probable. Another fairly constant lesion in animals that have died of rabies, but usually absent if they have been killed before the disease has run its full course, are the changes in the peripheral cerebrospinal ganglia, especially the plexiform ganglia of the pneumogastric nerves, described by van Gehuchten and Nélis. These changes consist in destruction of the normal large nerve-cells and their replacement by accumulations of small round cells, probably derived from the surrounding capsule.

The infection of rabies, whatever its nature, is not disseminated by the blood or lymph, but travels from the point of inoculation up the nerve-trunks to the central nervous system, and slowly produces in transit a toxin to which the medulla seems to be especially sensitive.

**Symptoms.**—The incubation period is usually about 6 weeks, but it may be as short as 2 weeks and very rarely it may be a year or even longer. The earliest symptoms appear toward the close of the incubation period and consist of general malaise, mental depression, restlessness, and a peculiar apprehensiveness, even if the patient does not know that he is in danger of rabies. At this time there may also be some evidence of irritation at the site of the wound. The temperature is often slightly elevated, although it may remain normal throughout. In the course of a day or two huskiness of the voice develops, with a slight choking sensation, and then violent spasms of the muscles of deglutition and respiration occur, with complete dysphagia, sensations of extreme dyspnea, and great mental anxiety. At first the paroxysms arise only with attempts to drink, and the dread of them soon results in a disposition to refuse water (hydrophobia). Later the general hyperesthesia becomes so pronounced that every trivial irritation, such as a draft of air or sudden noise, brings on spasms, and eventually these lose their local character and become more or less general. During the convulsive attacks there may be regurgitation of saliva and also a peculiar gasping, which to the popular mind may suggest the bark of a dog. Between the attacks the mental state is usually one of increasing mental agitation and apprehensiveness, but sometimes maniacal delirium supervenes. Death from exhaustion or asphyxia may occur within two or three days, while the patient is still in the convulsive stage. In the majority of cases, however, the convulsions finally cease, a general paralytic condition sets in and death occurs on the 3 rd or 4th day, usually in coma. Occasionally, especially after extensive bites, there are no convulsive features, but the disease throughout is of a paralytic type.

**Diagnosis.**—An animal that has bitten a person, if only suspected of having rabies, should not be killed immediately, but kept under observation, because if actually rabid it will always die in a few days with the symptoms of the disease. If at the end of two weeks it is still alive and well the possibility of rabies may be dismissed. After the death of the animal, natural or premature, the most reliable means of diagnosis is the production of the disease in a rabbit by intracerebral inoculation of an emulsion of the brain or medulla, although animal inoculation is virtually useless in determining the necessity for preventive vaccination, as characteristic symptoms rarely develop in animals in less than 2 weeks, and vaccination to insure the best results must be begun within a week following the bite. Fortunately, a histological diagnosis can be made very rapidly in the large majority of cases by the demonstration of Negri bodies in the large cells of the central nervous system. These bodies, which are now regarded as specific, appear early in the disease, and moreover are not readily affected by putrefactive changes.

The diagnosis of rabies in man is rarely difficult except in cases in which the bite has been overlooked or forgotten. *Tetanus* usually begins with trismus, produces persistent rather than intermittent muscular spasms, is often accompanied by opisthotonos, does not involve especially the muscles of deglutition and respiration, and lacks the peculiar mental features of hydrophobia. A condition known as *lyssophobia* or *pseudohydrophobia* is not infrequent in neurotic persons who have been bitten by supposedly rabid dogs. It may simulate hydrophobia, but the symptoms usually develop earlier than those of genuine rabies, there is often an obvious imitation of a dog, especially as to barking and attempts to bite, true respiratory spasm does not occur, and the condition commonly lasts longer than rabies and is amenable to anti-hysteric treatment.

**Prognosis.**—Once developed rabies is invariably fatal and usually terminates between the second and fourth days, but prompt and thorough cauterization of the wound and early vaccination after the method of Pasteur have reduced the incidence of the disease in persons who have been bitten by rabid dogs to less than 1 per cent.

**Treatment.**—Experience has shown that rigid enforcement of muzzling regulations, the destruction of ownerless dogs, and the quarantining of all dogs imported from countries in which rabies still exists are sufficient to stamp out the disease.

Any wound in which there is a suspicion that the animal inflicting it may have been rabid should be freely opened and thoroughly cauterized with fuming nitric acid. Cauterization alone, if done properly, will reduce the liability to rabies at least 50 per cent., and even if delayed for 36 or 48 hours, is of definite value. As soon as the diagnosis of rabies in the animal inflicting the wound has been clearly established, or at once if there is a strong suspicion that it is rabid, the patient should be given the benefit of the Pasteur treatment, which is most effective when begun within one week of the bite. The Pasteur treatment is a process of active immunization consisting of a series of subcutaneous injections of emulsions of tissue (spinal cords of infected rabbits) in which the virus has been "fixed" or attenuated by drying. The injections are made every day for a period of from 15 to 21 days, according to the nature of the wound, and each day the degree of attenuation of the virus is lessened.

If the bite has been produced by an animal certainly rabid, it is advisable to repeat the course of treatment after six months, so as to avert infection in case the particular virus has an exceptionally long incubation period.

While in the vast majority of cases the Pasteur treatment is harmless it is not wholly without danger. Occasionally it is followed in from 1 to 3 weeks by a paralytic condition, which in some cases is apparently a myelitis and in others a peripheral neuritis. Of 150 cases of paralysis, death occured in 25 (Remlinger).[1] When symptoms of rabies have appeared, the treatment is merely palliative. The patient should be kept in a quiet darkened room and made as comfortable as possible. If there is marked dysphagia recourse must be had to rectal feeding. To control the convulsive paroxysms it is often necessary to use injections of morphin or inhalations of chloroform.

[1] Ann. de l'Inst. Pasteur, 1905, 19, 6215.

## FOOT-AND-MOUTH DISEASE

(Epidemic Stomatitis; Aphthous Fever; Epizoötic Aphtha)

**Definition.**—Foot-and-mouth disease is an acute, specific, infectious and highly contagious disease occurring in cattle, hogs, sheep and goats, transmissible to man, and characterized by more or less constitutional disturbance and a vesicular eruption on the buccal mucous membrane and sometimes on the skin, especially that of the digits.

**Etiology.**—Epidemics occur more frequently in summer than in winter. The disease is transmitted from one animal to another by direct inoculation or through the medium of contaminated food or bedding. The affected animals develop vesicles in the mouth, as well as on the skin, and give evidence of moderate constitutional disturbance. In cows the udders and teats are not rarely affected. In man the disease is acquired usually through the ingestion of contaminated milk or milk products and only rarely by direct contact with an infected animal. The causative agent has not been isolated, but it is probably of the ultramicroscopic type (Loeffler and Frosch.[1])

**Symptoms.**—The period of incubation is from 2 days to 2 weeks. The earliest manifestations are chilliness, malaise, muscular pains, moderate fever, and a sense of heat in the mouth, with redness and swelling of the mucous membrane. Colicky pains, nausea and vomiting may also occur. In the course of two or three days, discrete vesicles appear in the mouth and on the lips, somewhat less frequently on the dorsal surface of the hands and feet, and occasionally on the face, breasts, genitalia, buttocks, or elsewhere. The eruption in the mouth is accompanied by salivation, dysphagia and swelling of the submaxillary lymph-nodes. After a few days the vesicles rupture, leaving shallow ulcers, which gradually heal without scar formation. The duration of the disease is from two to four weeks. One attack does not always confer lasting immunity. Recovery almost always ensues, but occasionally there is severe toxemia. Fatal cases occurred in several of the German outbreaks (Siegel[2]).

**Prophylaxis and Treatment.**—In man, *prophylaxis* consists in isolating the patient, disinfecting the secretions from the mouth and all articles soiled therewith, and avoiding milk and milk products from infected cattle. As an additional safeguard, during the prevalence of an epidemic among cows, all milk should be boiled. *Treatment* consists in using antiseptic mouth washes and in applying silver nitrate or copper sulphate to the oral ulcers and drying powders to the cutaneous lesions.

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## SPRUE

(Psilosis; Hill Diarrhea)

Sprue is a chronic disease, chiefly of tropical and subtropical countries, characterized by intermittent diarrhea and a peculiar form of stomatitis. It is especially prevalent in the Malay Peninsula and the adjacent countries, although it is reported from virtually all tropical and subtropical countries, including the southern portion of the United States. Apparently it attacks foreigners more frequently than natives. In temperate regions it occurs principally in persons who have spent some time in the tropics. Sprue may

[1] Centralbl. f. Bakteriol., 1897, xxii, 256.
[2] Deutsch. med. Woch., 1891, xvii, 1328.

be primary or may supervene upon other diseases of the digestive tract. The cause is unknown. Bahr[1] and a number of other writers believe that it is due to infection with a yeast fungus, *Monilia albicans*, but this view has not been generally accepted.

**Symptoms.**—In the early stages there are recurring attacks of stomatitis, characterized by marked tenderness of the gums and tongue and the occurrence of painful aphthous ulcers. Later, the tongue becomes red, bare, glazed and fissured. For a long time the diarrhea occurs chiefly in the early morning. The stools are large, pale, frothy and offensive, and are accompanied by much flatulence. They are also abnormally rich in neutral fat. Digestive disturbances are usually present, but they are overshadowed by the intestinal symptoms. A complete absence of hydrochloric acid in the gastric contents and of the pancreatic enzymes in the duodenal contents and stools has been observed in a number of instances (Brown,[2] Bovaird[3]). Occasionally, stomatitis is absent. The course of the disease is slow and marked by remissions and exacerbations. Eventually emaciation and pronounced anemia supervene, the blood changes sometimes resembling those of pernicious anemia. In advanced cases tetany may occur as a complication (Bassett-Smith,[4] Barach and Murray[5]).

*Hill diarrhea* is considered by some authorities to be identical with sprue, but it lacks the mouth symptoms of the latter and occurs almost exclusively at elevations of several thousand feet.

**Treatment.**—Unless the patient is thoroughly treated before the disease is far advanced, the outlook is gloomy. Prolonged rest and change of diet are the important therapeutic measures. Ordinary astringents are without effect. Cantlie[6] recommends moderate doses of castor oil every morning for three days and a purely meat diet of 5 ounces of minced beef, slightly broiled, three times a day for several days, with plenty of meat jelly and water in the intervals. Subsequently, fresh strawberries, *ad libitum* between meals, are said to be of service. On the other hand, Manson and others have had good results with a rigid milk diet. Preparations of pancreatic enzymes have been very beneficial in some cases. Lindeman[7] has employed transfusions of blood (1200 mils at weekly intervals) successfully in several instances. If the disease persists despite all treatment change of residence should be recommended.

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## OROYA FEVER

(Carrion's Disease[8])

**Definition.**—Oroya fever is an infectious disease, occurring in the mountain valleys of Peru, probably transmitted through the bite of an insect, and characterized by irregular fever, generalized pains, rapidly developing anemia, and extreme prostration. Until recently the disease was believed

[1] Brit. Med. Jour., July 25, 1914.
[2] Amer. Jour. Med. Sci., April, 1921.
[3] Jour. Amer. Med. Assoc., Sept. 3, 1921.
[4] Lancet, Feb. 1, 1919.
[5] Jour. Amer. Med. Assoc., Mar. 20, 1920.
[6] Brit. Med. Jour., Nov. 11, 1905.
[7] Jour. Amer. Med. Assoc., 1919, lxxiii, 897.
[8] In 1885 Daniel Carrion, a medical student of Lima, inoculated himself with blood from a Peruvian wart and in consequence died from a disease which was believed to be Oroya fever.

to be the first stage of verruga peruviana, but Strong and his co-workers[1] conclude from their investigations that the two conditions are distinct.

**Etiology.**—Oroya fever appears to be confined to certain narrow valleys on the Andes, between the ninth and sixteenth parallels of latitude, and at an elevation of 3,000 to 10,000 feet. It prevails especially toward the close of the warm, rainy season. The cause of the disease is not known, but Strong and his colleagues of the Harvard Commission believe it to be the rod-shaped organism (*Bartonia bacciliformis*), probably a protozoön, which they found in the red blood cells of Oroya fever patients. Thus far the virus, unlike that of verruga, has not been successfully transmitted to lower animals. A gnat of the Phlebotomus family may be the transmitting agent.

**Morbid Anatomy.**—The body is emaciated and extremely pale. The superficial lymph-nodes are swollen. Petechial hemorrhages are frequently found in the mucosæ and beneath the serous membranes. The liver is enlarged and flabby and often shows areas of toxic degeneration. The spleen is usually enlarged and may present numerous infarctions. Superficial ulcerations may be found in the large intestine.

**Symptoms.**—The period of incubation is said to be about 20 days. The onset is characterized by chilliness, malaise, severe pains in the head, back and limbs and fever. The temperature is irregular, fluctuating usually between 100° and 102° F., the tongue is coated, the liver and spleen are often enlarged, the superficial lymph-nodes are almost always swollen, the urine is scanty and occasionally albuminous, and as the disease progresses restlessness, insomnia and delirium may supervene. A characteristic feature is the rapid development of anemia of the pernicious type, with extreme prostration. The number of red corpuscles may be reduced to 1,000,000 per cubic millimeter or less. Nucleated red cells and poikilocytes appear early in the peripheral circulation. Leucocytosis (15,000–20,000) is the rule.

The mortality of Oroya fever is from 30 to 40 per cent. Death frequently occurs within 3 or 4 weeks of the onset. In favorable cases convalescence usually begins within 4 or 5 weeks.

**Treatment** is purely symptomatic.

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## VERRUGA PERUVIANIA

Verruga is an infectious disease occurring in the valleys situated on the slopes of the Peruvian Andes and characterized by a granulomatous eruption resembling that of yaws.

The causative agent is not known, but it can be transmitted from person to person and also to monkeys by direct inoculation. Townsend[2] suggests that in nature the transmitting agent is a species of biting gnat (*Phlebotomus verrucarum*).

Verruga is probably not, as was formerly believed, a stage of Oroya fever, but a distinct disease.

**Symptoms.**—The characteristic feature is the eruption, which is especially marked on the face and extensor surfaces of the limbs. It begins as an exanthem of red macules, which become papular and later develop into wart-like excrescences. The latter may not exceed the size of a small pea (miliary type), but not rarely they are as large as a hazel nut or larger (nodular type). The lesions, especially the larger ones, are very vascular and show a marked

[1] Jour. Amer. Med. Assoc., Nov. 8, 1913.
[2] Jour. Amer. Med. Assoc., Nov. 8, 1913.

tendency to bleed. Occasionally the miliary eruption involves the mucous membranes of the eyes, nose and throat. After lasting several months, the eruption may disappear by involution or by ulceration. The chief constitutional symptoms are articular pains, slight fever, and moderate anemia. The mortality is low.

## GANGOSA

(Rhinopharyngitis Mutilans)

Gangosa[1] is a chronic, specific ulcerative process, apparently of a granulomatous nature, involving primarily the pharynx, and extending to and tending to destroy the hard palate, larynx, nose and eyes. After a variable period, usually one or two years, the mutilation is likely to cease, although in some cases the process again becomes active. The disease prevails extensively in Guam and is found to a certain extent also in the Ladrone Islands, the Philippines, Fiji, and the West Indies. The infectious agent has not been isolated. Some observers look upon gangosa as a late manifestation of yaws, and others maintain that it is an expression of syphilis. The Wassermann reaction is frequently positive. Leprosy and lupus may usually be excluded by their more chronic course. The treatment is that of syphilis.

## TSUTSUGAMUSHI

(Japanese River Fever)

**Definition.**—Tsutsugamushi is an acute infectious disease, occurring in the western part of the island of Nippon, caused by the bite of a larval mite, and characterized by a small necrotic ulcer at the site of the bite, enlargement of the regional lymph-nodes, a macular eruption and a continuous fever, lasting about three weeks.

**Etiology.**—The disease is supposed to be confined to Japan, although a similar infection has been reported from Sumatra and the Philippines. The disease is not directly contagious, but acquired through the bite of an infected larval mite—*Trombidium akamushi.*

**Symptoms.**—The period of incubation is from 5 to 7 days. The first indication is the development of a small necrotic ulcer, with a red areola, at the site of the bite, which is usually about the genitals, the axillæ or the neck. The regional lymph-nodes soon become swollen and tender, and about a week after the reception of the bite constitutional symptoms consisting of chilliness, headache, vertigo, injection of the conjunctivæ, general hyperesthesia and fever supervene. On the sixth or seventh day after the onset a dusky macular rash appears on the cheeks, chest, trunk, forearms and legs and persists for five or six days. The temperature rises rapidly to 103° or 104° F., continues high until about the tenth day from the appearance of the eruption, and then falls by lysis. Cough is often present and delirium is not uncommon. The spleen is usually enlarged. The average mortality is from 20 to 30 per cent.

The **treatment** is entirely symptomatic.

[1] Spanish word meaning muffled voice.

## PHLEBOTOMUS FEVER

(Pappataci Fever; Three Day Fever)

**Definition.**—Phlebotomus fever is an acute infectious disease, acquired through the bite of a moth midge and characterized by a sudden onset, generalized pains, and fever lasting about three days.

**Etiology.**—The disease has been especially studied in the Balkan States, where it prevails epidemically, but doubtless it exists elsewhere. Outbreaks occur chiefly during the summer. The inciting agent is apparently a filterable virus and the transmitting agent a moth midge—*Phlebotomus papatassii*. The insect becomes infective in from 6 to 8 days after feeding on a patient in the first day of the disease. One attack usually produces lasting immunity.

**Symptoms.**—Clinically, phlebotomus fever is indistinguishable from *sand-fly fever* of India and Egypt. The period of incubation is from 3 to 7 days. The onset is very sudden and marked by headache, pains in the postorbital region, back and limbs, suffusion of the eyes, pronounced malaise and fever. The temperature rises rapidly to 103°, 104° or even 105° F. over a period of three days and then falls to normal. Mental depression, cough, and profuse sweating are frequently noted. The bowels are, as a rule, constipated. The blood shows leucopenia. The termination is favorable and the patient is usually well within ten or twelve days, although in some instances the disease is followed by more or less debility lasting several weeks. The short duration of the fever and the absence of characteristic articular and breakbone pains and of eruption may serve to distinguish phlebotomus fever from dengue, and the absence of pronounced catarrhal symptoms to exclude influenza, but the resemblance to both of these diseases is close. **Treatment** is symptomatic.

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## MILK SICKNESS

(Trembles)

**Definition.**—Milk sickness is an acute infectious disease of cattle, communicable to man, and characterized by gastrointestinal irritation, muscular weakness, and varied nervous disturbances.

**Etiology.**—The disease was formerly very prevalent in the newly settled regions of the Mississippi Valley and Southern States, but with advancing civilization and cultivation of the land, it has almost entirely disappeared. At present it is limited to a few localities in the mountains of North Carolina and Tennessee.

The causative agent has not been isolated. In man infection is acquired through the ingestion of milk or milk products or the flesh of animals sick with the "trembles."

**Morbid Anatomy.**—In the few necropsies that have been made the chief pathologic findings were injection and contraction of the stomach and intestines, enlargement and softening of the liver and spleen, ecchymoses in the serous membranes, marked congestion of the meninges, inflammation of the pia mater and softening of the brain.

**Symptoms.**—In cows the chief manifestations are a peculiar fetor of the breath, injection of the eyes, muscular weakness with tremor upon motion,

and, in severe cases, inability to stand and general convulsions. In some cases the disease remains latent until the animal undergoes some unusual exertion. In man the earliest symptoms are chilliness, headache, pain in the limbs and muscular weakness. Digestive disturbances soon supervene, the most common being anorexia, a peculiar sweetish odor of the breath, vomiting of frothy, bile-stained material, epigastric tenderness and obstinate constipation. The temperature is usually normal or but slightly elevated. The nervous symptoms may consist of extreme restlessness, delirium and convulsions, or of somnolence, stupor and coma. Death may occur in from a few days to a week or there may be a gradual abatement of the symptoms and a slow convalescence. In some epidemics the mortality has been 90 per cent.

**Treatment.**—This should consist of rest in bed, a soft diet, free purgation, and the use of stimulants, if necessary. Intrarectal or intravenous injections of normal salt solution would probably be of service.

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## RAT-BITE FEVER

Rat-bite fever is a specific infectious disease following the bite of a rat and characterized by recurring paroxysms of fever and a local or diffuse bluish-red eruption. It is best known in Japan, but cases have been reported from China, India, England and the United States. Although Schottmüller and others have ascribed the disease to a streptothrix (*S. muris ratti*), it is more likely that the actual etiologic agent is the protozoön, *Spirochæta morsus-muris*, which has been cultivated from the blood and tissues of patients by Futaki,[1] and others. According to Kusama,[2] and his co-workers the spirochete does not pass out through the saliva of the biting rodent, as is currently believed, but escapes from the submucous tissue or the circulating blood through an abrasion in the mouth of the animal.

**Symptoms.**—The wound heals readily, but after an incubation period varying from a few days to a month inflammation sets in and the regional lymph-nodes become swollen. Soon after the occurrence of these local changes an intermittent type of fever develops, the paroxysms of which last a few days, end by crisis, and recur about once a week over a period of many weeks or months. The fever is accompanied by muscular pains, chills, sweats, depression, etc., and a characteristic rash. The latter consists of a sharply defined bluish-red erythematous patch at or near the site of the bite or of widely disseminated bluish-red spots, varying in size from that of a pea to that of a silver half dollar. Cases of an abortive type, with slight fever, and others with a more or less continuous fever and marked nervous symptoms have also been described. It is difficult to find the spirochetes in the blood, as they are few in number, but they can be demonstrated satisfactorily by animal inoculation. In the past about 10 per cent. of the cases have terminated fatally, usually during the first febrile paroxysm.

**Treatment.**—Immediate and thorough cauterization of the wound is said to be a sure preventive. According to recent observations, the established disease usually yields readily to arsphenamin, which is a point in favor of the view that the causative agent is a spirochete.

[1] Jour. Exper. Med., 1917, xxv, 33.
[2] Arch. Exp. Med., 1919, 3, 131.

## MILIARY FEVER

(Sweating Sickness)

**Definition.**—Miliary fever is an acute infectious disease, occurring in localized epidemics of short duration, and characterized by fever, profuse sweating, and an eruption of miliary vesicopapules.

The disease prevailed epidemically in Europe at frequent intervals until the latter half of the nineteenth century. At present it is rare, although local outbreaks have recently occurred in northern France, Belgium, Switzerland and Austria. It has never appeared in the United States.

**Etiology.**—Miliaria is virtually limited to rural districts and usually appears in the spring or summer months. It attacks persons of all ages, but occurs more frequently in females than in males. It is probably contagious, but neither the inciting agent nor its manner of conveyance is known.

**Symptoms.**—The onset is usually sudden. Excessive sweating may be the first obtrusive symptom or, preceding this by a few hours, there may be chilliness, malaise, headache, muscular pains, and nausea and vomiting. The temperature ranges, as a rule, between 102° and 103° F., but hyperpyrexia has not rarely been observed. The pulse is accelerated out of proportion to the degree of fever, and other characteristic features are attacks of palpitation and of respiratory oppression and a peculiar sensation of epigastric constriction. Other nervous phenomena, especially mental anxiety and muscular cramps, are also common, and occasionally delirium and convulsions occur. The rash appears on the third or fourth day and consists of a diffuse erythema, with miliary papules, which later are transformed into minute vesicles. The mucous membrane of the mouth and nose is sometimes involved. In the course of a few days the rash dissappears and is followed by desquamation. With the occurrence of the eruption the fever, sweating and nervous disturbances gradually subside. Recovery is the rule, but the disease often results in considerable anemia, weakness and emaciation, and convalescence is usually slow. Relapses are common. Death may occur, even before the appearance of the rash, as a result of an increasing intoxication, with delirium, coma, convulsions, hemorrhages, etc. The mortality in different outbreaks has varied from zero to 33 per cent.

The **treatment** is purely symptomatic.

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## GOUNDOU

Goundou is a rare disease occurring chiefly among the natives of West Africa and characterized by persistent headache, a purulent nasal discharge and the development of symmetrical painless swellings (bony exostoses) at the sides of the nose near its root. It commences in childhood and by adult life the swellings are sometimes so large that they obstruct the lines of vision. The disease has been variously ascribed to yaws, to syphilis, to rhinoscleroma and to the presence of the larvæ of insects in the nostrils, but no etiologic theory has thus far found general acceptance. The treatment is surgical.

## AINHUM

Ainhum is a chronic process resulting in spontaneous amputation of certain toes or fingers, usually the little toe. It may occur in one foot only or in both feet. The disease has been observed most frequently on the western coast of Africa, in India and in Brazil, and is said to attack chiefly negroes of the male sex between the ages of 25 and 35 years. Whether it is a tropho-neurosis, an infectious condition, or a process excited by frequent injuries is not known. Clinically, a fissure occurs at the root of the toe on the plantar surface, deepens and gradually spreads until the member is completely encircled. The strangulation that ensues seems to depend upon hyperplasia and ingrowth of the epithelium and the formation of a ring of fibrous tissue. The toe beyond the point of constriction becomes enlarged and bulbous, and after a period ranging from 2 to 10 years drops off. Pain is usually absent until late in the disease. The absence of preliminary lesions, such as macules, tubercles, bullæ, etc., serves to distinguish it from leprosy, and the slow course and absence of pain are sufficient to exclude Raynaud's disease.

**Treatment.**—In long-standing cases the affected member should be amputated. In the early stages free scarification of the constricting band, followed by the application of an ointment of salicylic acid, may prevent further mutilation.

# NON-BACTERIAL FUNGUS INFECTIONS

The infections of this group comprise those due to molds—Hyphomycetes, to certain other filamentous organisms closely related to the molds—Trichomycetes, and to yeasts (budding-fungi)—Blastomycetes. Three cutaneous diseases due to pathogenic fungi have long been known, namely favus, caused by *Achorion Schönleinii;* ringworm, caused by two or more varieties of *Tricophyton;* and tinea (pityriasis) versicolor, caused by *Microsporon furfur.* There is still much difference of opinion, however, concerning the botanical position of the fungi found in association with these dermatomycoses. While many species of molds appear to be non-pathogenic in man, several are known to be capable of provoking disease. Among molds of the genus *Mucor,* one species, *Mucor niger,* has been thought to be the cause of the rare condition described as "black tongue." A case of generalized mucor infection, with intestinal ulceration and abscesses in various parts of the body, has been reported by Paltauf.[1] Instances of infection with several species of molds of the genus *Aspergillus* have been somewhat frequently reported, especially in France. Many of the cases have been in those who have had to do with the care of pigeons, these birds being particularly liable to aspergillosis. In the pigeon the disease appears as a pseudomembranous affection of the air-passages or as a chronic bronchopneumonia. In man it attacks chiefly the lungs, producing lesions similar to those of tuberculosis (pulmonary aspergillosis). A species of *Sporothrix* (Sporothrix schenckii-beurmanni) is sometimes found in association with certain pathologic conditions. The skin, especially that of the arm and hand, is usually the seat of the lesions, although the parasite may attack the bones or joints, the mucous membranes, or the lungs. In the skin the lesions are likely to be confused with cutaneous gummata, cutaneous tuberculosis or staphylococcic abscesses.

Our knowledge of the biology of the Trichomycetes is still meager, and for this reason much perplexity has arisen in classifying and naming these parasites. Jordan[2] suggests the following classification: (1) Leptothrix, characterized by an absence of branching; (2) Cladothrix, characterized by "false" branching, the division of a terminal cell often giving the appearance of branching; (3) Nocardia[3] characterized by true branching and the formation of spores; and (4) Actinomyces, characterized by true branching, but no formation of spores.

Species of *Leptothrix* are frequently found as harmless saprophytic parasites in the mouth and in the vagina, and in a number of instances organisms of this class seem to have been responsible for suppurative processes in various parts of the body, especially about the mouth and throat. Organisms of the *Nocardia* group have been described by Nocard as the pathogenic factor in "farcin du bœuf," a tubercle-like affection of the superficial lymph-nodes of cattle. Similar forms have been found in cerebral abscess (Eppinger, Almquist, and Sabrazès and Rivière), and not infrequently in chronic pulmon-

[1] Archiv. f. path. Anat., 1885. 102.

[2] Jordan, General Bacteriology, seventh edit., p. 517.

[3] Sometimes termed Streptothrix, a name that has also been applied to the whole group of Trichomycetes.

ary affections closely simulating tuberculosis. *Actinomyces* is the specific organism of actinomycosis of cattle and man, a disease that has been more thoroughly studied than any of the other non-bacterial fungus infections. It has been thought that the actinomyces leads a saprophytic existence on blades of grass and the ears of various cereals and that infection is accomplished by direct implantation of the parasite in the tissues, especially the mucous membrane of the mouth or throat, through an abrasion. It has not been clearly proved, however, that the filamentous fungi found on barley and other grains are identical with the true actinomyces. A species of actinomyces, or a filamentous fungus with similar characteristics, is also the cause of at least one variety (white) of mycetoma, or Madura foot.

As Gilchrist first pointed out (1894), blastomycetes, or yeast-like fungi, are concerned in the production of a peculiar form of dermatitis, known as cutaneous blastomycosis, and which in many cases is clinically suggestive of cutaneous tuberculosis or lupus vulgaris. In some instances, even in the absence of cutaneous lesions, systemic infection occurs, the lungs being chiefly involved and the symptoms and physical signs of the disease closely resembling those of pulmonary tuberculosis. Finally, the yeast-like organism commonly known as *Oïdium albicans* has long been recognized as the specific cause of parasitic stomatitis, or thrush.

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## ACTINOMYCOSIS

**Definition.**—Actinomycosis is a chronic infectious disease caused by the *Actinomyces*, or ray-fungus, and characterized by the formation of tumor-like masses of inflammatory tissue, which ultimately soften and discharge a puriform liquid containing small granules of a sulphur-yellow color, made up of the fungus.

**Etiology.**—Actinomycosis is most frequently seen in cattle in whom it affects especially the jaw or tongue, producing what is known as "lumpy jaw" or "wooden tongue." It is comparatively rare in man. The specific cause of the disease occurs in the form of clusters or rosettes, consisting of a central mass of threads and peripheral rays with club-shaped terminations. Whether the parasite normally lives in the mouth or has its natural habitat outside of the body on grains, especially barley, as Bostroem and others have claimed, remains to be demonstrated. The frequency with which the jaws and adjacent parts are affected speaks strongly of oral infection, probably through an abrasion of the mucous membrane or a carious tooth. No instance of direct transmission of the disease from the sick to the well has been recorded.

**Pathology.**—The lesion produced by the Actinomyces consists of a central area of liquefaction necrosis with an accumulation of leucocytes, surrounded by an extensive zone of granulation tissue and an outside layer of fibrous tissue, the whole forming a tumor-like mass, which gradually increases in size, bores into adjacent structures, and finally ulcerates through to the surface of the body, discharging its puriform contents through fistulous tracts and sinuses. In the puriform fluid are found the characteristic sulphur-yellow granules, just large enough to be visible to the naked eye and composed of actinomycelial clumps. Metastasis to the internal organs is sometime observed, and when it occurs the blood rather than the lymph seems to be the medium by which the disease is disseminated.

**Symptoms.**—Actinomycosis involves the *head* and *neck* in somewhat more than half of the cases. It is characterized by the gradual development of an indurated swelling, usually in the submaxillary or parotid region, which at first may resemble a sarcoma, but eventually suppuration occurs and pus containing the peculiar granules is discharged through fistulous openings on the neck or cheek. In long-standing cases the jaw-bone is riddled with sinuses which communicate with one another and with the exterior. The regional lymph-nodes are rarely enlarged except from secondary pyogenic infection. The latter also is responsible for the impairment of the general health rather than the actinomycosis itself.

The *lungs* are involved in about 15 per cent. of the cases, the disease occurring as a chronic bronchitis with fetid sputum, as a chronic bronchopneumonia or plueropneumonia, or, rarely, as miliary actinomycosis. The resemblance to pulmonary tuberculosis may be very close. The chief points of distinction are the presence of the characteristic fungus in the sputum instead of the tubercle bacillus, the predilection of the lesions for the bases, the exceptional rarity of hemoptysis, and the tendency to form subcutaneous abscesses with fistulous openings. The *abdominal organs* are affected in about 20 per cent. of the cases. A favorite site is the ileocecal region of the bowel, the disease being usually confused with tuberculosis or carcinoma of the cecum or with a psoas abscess. The diagnosis before perforation can be made only by finding the Actinomyces in the stools. The liver is not rarely the seat of secondary abscesses, the infection being conveyed to the organ by direct continuity or by metastasis through the bloodstream. A number of cases of secondary actinomycosis of the ovary are also on record.

Actinomycosis of the *skin* is sometimes observed, but it is usually on the neck or face and secondary to infection of the mouth. Primary invasion of the skin is rare. It is characterized by the formation of dark red nodules, which eventually break down and form chronic sinuses or indolent ulcers. Invasion of the *brain* is extremely rare and is clinically indistinguishable from cerebral abscess or tumor. All forms of the disease are accompanied by weakness and emaciation, and pyemic symptoms often arise as the result of secondary pyogenic infection.

**Diagnosis.**—The diagnosis can be made with certainty only by finding the specific parasite. Every chronic fistulous phegmon, however, should be regarded with suspicion, especially if it has a tendency to involve the bones and is located on a site particularly affected by the Actinomyces, such as the face, neck, thorax and iliac fossa.

**Prognosis.**—If the lesion is localized and so situated that it can be treated surgically the prognosis is favorable. In the internal forms the outlook is very gloomy, although occasionally a cure is effected. The average duration of the fatal cases is from one to two years. The reported mortality in the maxillary cases has ranged from 25 to 65 per cent. and that of the abdominal cases from 70 to 85 per cent.

**Treatment.**—The treatment of an accessible lesion is by complete excision, or if this is impossible, by partial excision or curettement, followed by the application of iodin or of phenol and alcohol. Internally, potassium iodid is of definite value and should be used in all cases irrespective of other forms of treatment. To secure the best results it should be given in large doses, as much as 3 drams (12.0 gm.) daily. Bevan has recommended cupric sulphate, internally in doses of ¼ to ½ grain (0.015–0.03 gm.) thrice daily, and locally in 1 per cent. solution. In the pulmonary form good results have been claimed for eucalyptus oil in spray and in capsules. A vaccine of

the homologous organism, prepared by cultivating the fungus in nutrient broth to which a few drops of fresh human blood have been added, has sometimes proved serviceable (Wynn,[1] Kinnicutt and Mixter,[2] Gordon[3]). Recently, roentgen ray or radium has been used in a number of cases with good results.

## MYCETOMA OR MADURA FOOT

Mycetoma is a chronic localized infection of the skin and underlying tissues, usually of the foot, due to certain species of fungi. It is especially prevalent in Madura, India, but it occurs in other parts of India, and cases have been reported from Africa, the West Indies, South America and the United States.

The malady affects the foot in more than 75 per cent. of the cases, and is characterized by edematous swelling and the presence of elevated nodules, which tend to break down and form sinuses. From the sinuses is discharged a viscid, slightly purulent liquid, containing small granules made up of the specific fungus. Three varieties of mycetoma are recognized according to the color of the granules: a white variety (most common) with pale yellowish-white granules, resembling fish-roe; a much less common black variety, with hard gunpowder-like granules; and a very rare red variety, with small reddish granules. The organism of white mycetoma resembles in appearance the Actinomyces, but its cultural features are distinctive. The parasite of the black variety is a much larger fungus with thick, branching filaments and transverse septa like the hyphæ of the higher molds (Wright).

The disease is not painful, it does not extend by metastasis to the internal organs, and in the absence of secondary infection it is not accompanied by fever or enlargement of the regional lymph-nodes. Its course is slow, but after a time, usually several years, the foot becomes greatly enlarged and distorted, and eventually all of the tissues of the affected area, even the bony structures, undergo disintegration. The patient not rarely lives ten or even twenty years, and when death occurs it is usually due to exhaustion or intercurrent disease. The diagnosis is based upon the location of the lesion, the absence of any tendency to visceral involvement, and, above all, the discharge of the variously colored granules, which upon microscopic examination are found to consist of filaments of the fungus. Cure can be effected only by complete removal of the diseased tissue by the knife or curet. Potassium iodid has been recommended, but apparently it is of no value.

## NOCARDIOSIS

**(Streptothricosis; Pseudotuberculosis)**

The term nocardiosis is applied to infections caused by *Nocardia*, filamentous fungi, which show both branching and spore-formation. Organisms of this group have also been termed *Streptothrix*, but this designation is less distinctive as it has been applied by some writers to the whole group of Trichomycetes.

[1] Brit. Med. Jour., 1908, i, 554.
[2] Boston Med. and Surg. Jour., 1912, 167, 90.
[3] Brit. Med. Jour., 1920, i, 435.

Infection by Nocardia, which is comparatively rare, is usually acquired by inhalation, but direct inoculation through wounds has been observed. The organisms have been found in abscesses in various situations, most frequently about the head and neck, although doubtless many of the cases recorded as nocardiosis would now be regarded as examples of actinomycosis.

When the disease attacks the respiratory tract, which appears to be the most common point of entrance, it produces lesions and symptoms very similar to those of pulmonary tuberculosis. In many of the recorded cases the only evidence against tuberculosis was the persistent absence of the tubercle bacillus. In this connection it must be noted that both nocardiosis and tuberculosis sometimes occur in the same patient. A positive diagnosis depends upon finding the mycotic parasite in the sputum. In stained specimens it appears in the form of slender filaments, which are often beaded. As many species are moderately acid fast, care must be taken not to mistake short fragments of filaments for tubercle bacilli. Claypole[1] using a glycerin bouillon culture of Nocardia as an antigen obtained a definite skin reaction in infected persons similar to that produced by tuberculin in tuberculosis. The outlook in pulmonary nocardiosis is grave. In the treatment potassium iodid should be given a thorough trial.

## BLASTOMYCOSIS

(Oïdiomycosis; Saccharomycosis)

Blastomycosis is a chronic infectious disease caused by Blastomycetes, or budding (yeast-like) fungi. It presents itself as a well-defined disease of the skin or as a general infection involving both the skin and the internal organs. The parasites are oval or round bodies, 10 to 15 $\mu$ in diameter, with a doubly contoured capsule and a finely granular and often vacuolated cytoplasm. Reproduction in the tissues occurs by budding, but in cultures by mycelial formations. Infection may occur by way of the skin or the respiratory tract, but nothing definite is known concerning the conditions leading to it. The lesions produced are nodules composed of granulation tissue, with, as a rule, numerous giant cells. More or less extensive suppuration occurs, but there is little or no tendency to caseation. In the skin there are marked epithelial hyperplasia and granulomatous infiltration of the corium, with minute epidermal abscesses. The Blastomycetes are present, usually in large numbers, between and within the cells of the nodules and in the pus.

**Cutaneous blastomycosis**, which is the more common form, begins as a small papule, which gradually enlarges and then softens and becomes covered by a crust. Removal of the crust reveals a red granulating surface with a somewhat verrucous appearance. The patches increase peripherally and when well developed are irregular in outline, elevated, reddish and covered with uneven papillary projections, separated by fissures or clefts. The borders are of a deep red tinge, sharply defined and studded with many minute abscesses. As the lesion advances, evidences of cicatricial healing frequently appear in the older parts. The regional lymph-nodes are not often enlarged. The two diseases which give rise to most difficulty in diagnosis are tuberculosis and lupus vulgaris. Microscopic examination of the affected tissue or of the pus is often necessary before a definite opinion can be

[1] Trans. Nat. Assoc. for the Study and Prevention of Tuberculosis, 1914.

given. The disease is chronic, lasting many years. It usually remains limited to the skin, but occasionally systemic infection supervenes. Recent and localized lesions yield, as a rule, to appropriate treatment. Recurrences, however, are not uncommon.

**Systemic blastomycosis** often presents a clinical picture closely resembling that of pulmonary tuberculosis, both in symptoms and physical signs. Sooner or later, however, foci are likely to appear in the skin, subcutaneous tissue, joints, or elsewhere. In other cases symptoms of an acute febrile condition first appear and are followed after a short time by the occurrence of superficial or deep abscesses. As the disease progresses, irrespective of its mode of onset, there is a gradual loss of weight and strength, with irregular fever, increasing anemia and leucocytosis. The diagnosis depends upon the detection of the specific fungus. Of 29 recorded cases only 4 terminated favorably. The average duration is from 1 to 2 years. After death one usually finds characteristic ulcers in the skin and yellowish nodules or abscesses of varying size in the subcutaneous tissue and internal organs. Foci in the joints or bones may also be found.

The treatment of cutaneous lesions consists in excision or curettement, *x*-ray applications, and the administration of iodids in large doses. Locally, solutions of iodin and of copper sulphate (1 per cent.) are recommended. In systemic cases iodids should be given in maximum doses. Hyde advocates 200 to 500 grains (12.0–30.0 gm.) daily. Stober has used a vaccine in a few cases with encouraging results.

**Coccidiodal Granuloma.**—The disease known as coccidiodal granuloma, which has been observed especially in the San Joaquin Valley, California, is closely related to, if not identical with, blastomycosis. General infection, however, seems to be the rule, and is almost invariably fatal. The causative organisms differ from the Blastomycetes chiefly in multiplying in the tissues by sporulation instead of by budding, although in pus and culture media budding has been observed.

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## SPOROTRICHOSIS

Sporotrichosis, or infection by spore-bearing fungi of the genus *Sporotrichum*, occurs as a local process affecting the skin, or much less frequently as a generalized systemic disease. It is comparatively rare, although cases are being reported in increasing numbers. Hamburger[1] has collected from American literature 58 cases, all of the cutaneous form. The large majority of the patients were residents of the region comprising the Mississippi River basin. De Bourmann and Gougerot[2] have added much to our knowledge of the subject.

**Cutaneous sporotrichosis** most frequently affects the hand and forearm. Farmers, florists, vegetable dealers, etc., seem to be the chief sufferers. A history of preceding trauma is often noted. The lesions are small, firm, painless nodules, which slowly enlarge and finally soften and form indolent ("cold") abscesses or break through the skin, discharging a viscid grayish-yellow pus and leaving fistulous openings or irregular crateriform ulcers. They sometimes follow the course of the deep lymphatics, which may be felt as hard cords. The disease is very chronic and shows no tendency to spontaneous recovery. It is most likely to be confused with tertiary syphilis,

[1] Jour. Amer. Med. Assoc., Nov. 2, 1912.

[2] "Les Sporotrichosis," 1912; also de Bourmann: Brit. Med. Jour., Aug. 10, 1912.

verrucous tuberculosis, blastomycosis, and staphylococcic abscesses. The diagnosis is best made by cultural methods, the organism growing readily on glucose agar or glucose peptone gelatin, forming a characteristic radiating, flower-like colony. Detection of the parasite by direct examination of the pus is difficult.

**Extracutaneous sporotrichosis** may be associated with the cutaneous form or occur as the sole expression of the infection. The localization may be in the muscles, mucous membranes, bones, or joints, or more rarely in the lungs or other viscera. In the muscles large gumma-like nodules may be observed. Of the mucous membranes, that of the bucco-pharynx is the one usually affected, the lesion appearing as a chronic simple or verrucous ulcer. In the bones sporotrichosis simulates closely syphilitic osteitis and in the joints, tuberculous, syphilitic or gonococcal arthritis. Sporotrichosis of the lungs, which is exceedingly rare, presents a clinical picture similar to that of pulmonary tuberculosis.

The disease usually responds more or less rapidly to large doses of potassium iodid. Ulcers are favorably influenced by local applications of dilute Lugol's solution. Except in large abscesses, surgical treatment is inadvisable.

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## PULMONARY ASPERGILLOSIS

Instances of infection with species of molds of the genus Aspergillus have been somewhat frequently reported, especially in French literature. Most of the cases have been among men whose business has been the mouth-to-beak feeding of pigeons ("gaveurs de pigeons"), but whether the infection was acquired directly from a diseased pigeon or from grain used in the feeding is not apparent. Infection also arises from other sources, but how it occurs is not definitely known. In some cases it has developed as a secondary process in the course of pulmonary tuberculosis.

The disease is extremely rare in this country. It produces lesions and symptoms similar to those of pulmonary tuberculosis and is to be distinguished only by finding the mycelial threads and spores of the fungus in the sputum. The outlook is grave, although arrest of the process sometimes occurs.

# METAZOAN INFECTIONS

## TÆNIASIS

### (Cestode Infestation)

According to Stiles man seems to be the normal and sole host for the sexual stage of at least two large tapeworms, *Tænia saginata* and *Tænia solium*. Man, together with the dog, probably forms the normal host for a third large tapeworm, *Dibothriocephalus latus*. In common with the rat man seems to have become a normal host for the dwarf tapeworm, *Hymenolepis nana* and for *Hymenolepis diminuta*. Occasionally man harbors other species of tapeworm.

### INTESTINAL TÆNIASIS

#### (Tapeworm Infestation)

**Tænia saginata (T. mediocanellata).**—The fat, unarmed or beef tapeworm is the most common tapeworm of man in North America and in most parts of Europe. The mature parasite is a white, flat, jointed worm, from 4 to 8 meters (12 to 25 feet) or more in length. The head (scolex) is square, as large as that of a pin, and is provided with four sucking discs, but no hooklets. The ripe segments (proglottides) measure 18 mm. by 7 to 9 mm. and may number 1000 or more. The uterus in the gravid segments has 15 to 35 slender dichotomous lateral branches each side of, and shorter than, the median stem. The common sexual aperature is marginal and placed alternately on the two sides. The eggs are brown, oval, about 30 to 40 feet long, and have an outer vertically striated envelope (embryophore). Usually only a single worm is present, although as many as twenty-five have been found.

Cattle become infected by swallowing the eggs in food or water contaminated with infected human feces. The larva (onchosphere) penetrates the intestinal wall, and lodging in the muscles, liver or viscera, becomes encysted (*Cysticercus bovis*). Man acquires the infection by eating raw or insufficiently cooked meat infected with cysticerci ("measles" of beef). The larval form requires 2 or 3 months to develop into the mature worm, and this may continue to infest its host for many years.

**Tænia solium,** the armed or pork measle-tapeworm, is a rare parasite in North America and Great Britain, but is found in Continental Europe and in Central and South America. It is somewhat smaller than the beef-tapeworm, not often measuring more than 2, 3 or 4 meters (6, 10, or 12 feet) in length. The head is rounded and provided with four cup-like suckers and a rostellum bearing a double circle of hooklets. The genital pores are marginal, as in the beef tapeworm, but the uterus in the gravid segments differs from that of the latter parasite, in having only half the number of lateral branches. The eggs resemble those of the beef tapeworm, except that they are almost spheric. Hogs become infected by swallowing human excrement containing the eggs or ripe segments of the worm, and, as in the case of T. saginata, the embryos pass into the muscles and organs to produce cystic larvæ (*Cysticercus cellulosæ*), the latter appearing as oval, whitish bodies, from the size of a hemp seed to that of a pea. Man becomes infested

by eating raw or undercooked pork infected with cysticerci (pork "measles"). Contrary to the usual rule, both the larvæ (cysticerci) and the adult worm may develop in man, the latter occasionally becoming self-infected by the eggs, which are accidentally transferred to the mouth by the hands or which gain entrance to the stomach through vomiting.

**Dibothriocephalus latus,** the broad or fish tapeworm, prevails especially in the vicinity of large bodies of water, and is a common parasite in Sweden, Russia, Denmark, Eastern Prussia, Switzerland and Japan. It occurs, however, elsewhere, as in Iceland, in South Africa, and in the United States, especially among the Finns and Swedes of Michigan and the adjacent states. In a few cases on record the patient unquestionably acquired the parasite in the United States. It is the largest of the tapeworms infesting man, a mature specimen often measuring from 8 to 15 meters (25 to 45 feet) in length. The head is club-shaped, unarmed, and has two narrow longitudinal suckers, one on each side. The segments, 3000 to 4000 in number, are usually broader than long.

The general aperature is central in the broad surface of the segments and the uterus is in the form of a rosette. The eggs are oval and provided at one pole with a distinct operculum or lid for the escape of the embryo (onchosphere) which is ciliated. The latter enters an unknown intermediate host, probably a mollusk, which transmits it in an ameboid form, without cilia, to fish (salmon, trout, pike, etc.). In the muscle or viscera of the fish it is transformed into an elongated larva (plerocercoid), measuring 1 to 2 cm. in length and 2 to 3 mm. in width. Man becomes infested by eating raw or undercooked fish. On reaching the intestine the procercoid larva attaches itself to the mucosa and in a few months attains the adult stage.

**Hymenolepis nana.**—The dwarf tapeworm is the smallest tapeworm infecting man, the full-grown parasite not often exceeding 30 or 40 mm. (1 or 1½ inches) in length. The head is rounded and provided with a rostellum, a single circle of hooklets, and four sucking discs. The genital pore is marginal. It is a common parasite in many parts of the world, and infestation occurs probably from food contaminated by the excrement of rats infected with the worm. Children are more frequently affected than adults. Auto-infestation is probable, as the life history of the worm is completed without any intermediate host and a large number of parasites are frequently found in one person.

**Hymenolepis Diminuta.**—This tapeworm is comparatively rare in man, but is common in rats. The adult parasite measures 20 to 60 cm. (8 to 25 inches) in length by only 3 or 4 mm. (⅛–⅙ inch) in width. The head is minute and provided with four suckers and a rudimentary rostellum without hooks. The anterior segments present a yellow spot (receptaculum seminis) and the posterior segments a brownish spot (matured uterus). The cysticercus stage has been found in fleas and other insects. Man and the rat become infested probably through eating food contaminated by insects.

**Symptoms of Intestinal Tæniasis.**—The symptoms are variable, depending upon the species of tapeworm, the size and number of the parasites, and the sensitiveness of the patient. In some cases they are not sufficiently marked to attract attention, the presence of the parasite being made evident only by the discovery of segments or fragments in the stools. Frequently, however, tapeworms cause more or less disturbance, both local and general. The local symptoms include uncomfortable sensations in the abdomen or actual gripping pain, itching at the anus and nostrils, furred tongue and foul breath, a capricious appetite, various digestive disturbances, and irregular action of the bowels. Attacks of vomiting are not uncommon, and occasion-

ally there is marked salivation. Certain kinds of food at times appear to increase the local symptoms.

Among the general manifestations which may be observed are a feeling of languor and weakness, depression of spirits, pallor, discoloration around the eyes, dull headache, giddiness and sometimes emaciation. Reports of epileptiform convulsions and other nervous disorders of a more or less grave character have also been made, but they must be received with caution. Vomiting is a dangerous feature if the tapeworm is Tænia solium, for should the segments be retained in the stomach the patient is liable to become infected with larval forms of the parasite (cysticerci).

Dibothriocephalus latus sometimes produces a severe anemia, simulating pernicious anemia, which has been attributed to a poison secreted by the living worm and also to a globucidal toxin liberated from dead segments of the parasite. According to Tallqvist[1] the hemolytic substance is a lipoid. The only way in which tapeworms can be recognized with certainty is by the discovery of their segments or eggs in the stools.

**Treatment.**—In every case it is advisable to precede the administration of the anthelmintic for two or three days by a spare diet, chiefly of liquids and eggs, and by the use of saline or other laxatives, so as to leave the worm with as little protection as possible by intestinal residue. Only coffee or tea should be allowed for breakfast on the day that the tenifuge is to be given, and about two hours after the administration of the latter, unless the bowel acts thoroughly meanwhile, a brisk purgative should again be used. For the day, at least, it is advisable for the patient to remain in bed, in order to avoid vomiting. The most effective remedies are oleoresin of aspidium, ½ to 2 drams (2–8 mils), divided into small capsules or with an agreeable syrup; pelletierin, the alkaloid of pomegranate, 6 to 10 grains (0.4–0.6 gm.), in the form of the tannate; decorticated pumpkin seeds, 2 or 3 ounces (30.0–90.0 gm.) made into an electuary by grinding with honey or jam; and cusso (kousso), 6 drams (24.0 gm.), in wine or in the form of an infusion. If aspidium is used, it should be followed by some other purgative than castor oil, as the latter favors absorption of the poisonous constituents of the drug.

As it is always important to know whether the head of the parasite has been expelled, the stools should be carefully preserved, then mixed with water, and filtered through coarse gauze. Should the worm come away slowly and be found hanging out of the anus its expulsion may be expedited by an enema of warm water. Traction on the worm should never be made. If the head is not found treatment should be repeated in 2 or 3 months, or when segments again appear in the stools. It is advisable to wait this long, because the head, owing to its small size, is not rarely overlooked.

Pregnancy, acute inflammation of the gastrointestinal tract, convalescence from acute infections, advanced cardiac or renal disease, and tuberculosis with a tendency to hemoptysis are contraindications to the treatment for tapeworm infection.

The most important prophylactic measures are (1) careful inspection of meats in abbatoirs, (2) thorough cooking of all meats, even of those that are smoked or salted, and (3) incineration of feces containing ova or segments of tapeworms.

## SOMATIC TÆNIASIS

Infection with the larval stage of tapeworms is chiefly due to the *Echinococcus granulosus* (hydatid disease) and the *Cysticercus cellulosæ* (cysticerco-

[1] Zeit. klin. Med., 1907, 61, 427.

sis), especially the former. Infection with *Sparganum mansoni* and *Sparganum proliferum* has also been observed among the Japanese.

**Echinococcus or Hydatid Disease.**—The adult form of the parasite lives in the small intestine of the dog or wolf, and the larval stage occurs in man, as well as in a number of domesticated animals. Man is infected by swallowing the eggs of the adult worm discharged in the feces of a dog. Escaping from the intestine the embryos may migrate to any part of the body, but most frequently they enter the liver. The embryo once at rest slowly develops into a *hydatid* or *echinococcus cyst*. The latter consists of an outer thick, translucent, laminated membrane—the ectocyst and an inner, thin, granular, germinal layer—the endocyst. From the endocyst originate small buds, which become "brood capsules" of immature heads of the adult parasite (scolices). If the wall of the brood-capsule is ruptured the scolices may become detached and float free in the contents of the mother cyst, which is a clear saline fluid, with a specific gravity of 1004 to 1013. As the parent cyst grows, daughter cysts and even grand-daughter cysts containing scolices with their characteristic hooklets may form and later become free in the hydatid fluid. In this way the original cyst may attain a weight of many pounds and contain scores or even hundreds of daughter cysts. As a result of spontaneous rupture or evacuative puncture of a primary hydatic cyst scolices may be set free and give rise to the formation of secondary cysts in surrounding tissues or organs.

In rare instances, probably through infection by a distinct species of parasite, *Echinococcus multilocularis*, there is formed the so-called *multilocular cyst*, which is a tumor-like mass consisting of numerous small cavities filled with gelatinous fluid and usually communicating with one another.

When dogs are fed on liver or other organs affected with echinococcus cysts, the scolices are liberated and on entering the small intestine each is developed into a mature tapeworm (*Tænia echinococcus*). The latter, which is rarely more than 5 mm. ($\frac{1}{6}$ inch) long, is composed of a head (scolex) with 28 to 50 hooklets, a short neck, and 3 or 4 segments (proglottides).

Echinococcus infection is especially common in Iceland, Australia and certain parts of Germany. In America and Great Britain it is comparatively rare.

*Location of Echinococcus Cysts.*—The cysts may occur in any part of the body, even in the heart, the bones and the eye, but the liver is involved in nearly two-thirds of all cases, the lungs in 10 per cent. and the kidneys in 8 per cent.

*Results.*—The effect of the cyst in the tissues is that of mechanical pressure and atrophy. As a result of irritation an external fibrous capsule is gradually produced. The duration is variable; often many years elapse before death occurs. Occasionally the parasites die and the cyst is reduced to a small cavity containing lime salts and detritus. Bacterial invasion sometimes takes place and the cyst in consequence is transformed into an abscess. The chief complication, however, is rupture of the cyst into adjacent organs or cavities. If the rupture does not prove immediately fatal, it may result in secondary inflammatory conditions or more rarely in the metastatic transportation of the infection to other organs, with the formation of secondary cysts. The most favorable perforation is externally through the skin. The rupture or leakage of a cyst is frequently attended by certain toxic phenomena (anaphylaxis), especially eosinophilia, urticarial rashes and shock.

*Symptoms.*—The symptoms are chiefly those of a slowly growing tumor, which may attain very large dimensions. The tumor may be more or less

elastic and occasionally it may even fluctuate. Superficial cysts rarely yield on percussion a peculiar quivering sensation, which is known as the "hydatid thrill." A roentgen-ray examination sometimes yields important information. Pressure symptoms are relatively uncommon and contrasted with the physical signs, the constitutional disturbance is usually very slight. Eosinophilia is sometimes observed. Serum diagnosis, according to the complement-fixation method, using the fluid of the cyst as antigen, has been of value in a considerable percentage of cases. The detection of scolices or hooklets in the fluid is, of course, certain evidence, but the danger of paracentesis as a means of diagnosis outweighs its advantages, and, as a rule, exploratory incision is preferable. In rare instances hydatids are discharged through the bowel, through the vagina, in the urine, etc.

An echinococcus cyst of the liver may rupture into the peritoneum, an adjacent hollow viscus, the bile-ducts, or the inferior vena cava, or it may perforate the diaphragm and invade the pleura, lung or pericardium. According to Dévé,[1] rupture into the peritoneum occurs in about 22 per cent. of the cases.

Echinococcus disease of the lung may present itself under the guise of neoplasm, tuberculosis, massive pneumonia, or pleurisy with effusion. Rupture may occur into a bronchus or into the pleura, causing pneumothorax or pyopneumothorax. Renal cysts frequently evacuate their contents through the pelvis of the kidney, producing attacks of pain simulating renal colic. In many cases the rupture results in spontaneous cure.

The only effectual *treatment* of hydatid cysts is surgical.

**Cysticercosis.**—The larval form of Tænia solium, *Cysticercus cellulosæ*, is an oval, translucent bladder-like structure, 6 to 12 mm. (¼ to ½ inch) in length. It develops in man from ova of the adult parasite which have reached the stomach through contamination of food or the hands, or, perhaps, through regurgitation during vomiting. Self-infection is sometimes noted, the patient harboring at the same time both the mature worm and larval forms. It requires about three months for ova to develop into cysticerci, and the latter may live for many years. In man the parasites are found in the subcutaneous tissues, muscles, brain, eye, heart, lymph-nodes, bones, etc. Large numbers are sometimes present. The infection is rare. In 1899 Diamond[2] was able to collect only 8 cases reported from America.

The symptoms vary with the location and number of the parasites and unless accessible regions are involved, such as the eye or the subcutaneous tissues, the diagnosis is scarcely possible. In a number of cases the parasites have been extracted from the eye.

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## NEMATHELMINTHIASIS

The chief representatives of the nemathelminthes, or round worms, are the *nematodes*, which include Ascaris lumbricoides (eelworm, common round worm), Oxyuris vermicularis (pinworm or seatworm), Trichuris trichiura (whipworm), Strongyloides stercoralis, Ankylostoma duodenale and Necator americanus (hookworms), Trichinella spiralis (trichina), and Filaria bancrofti and other species of filariæ.

[1] Dévé, F.: De l'echinococcose secondaire, Paris, 1901.
[2] Jour. Amer. Med. Assoc., June 17, 1899.

## ASCARIASIS

### (Eelworm Infection; Common Roundworm Infection)

The eelworm, *Ascaris lumbricoides*, is the most common of the intestinal worms infesting human beings. Infection may occur at any age, but is most frequent in childhood. The parasite is of a yellowish or reddish-gray color, pointed at both ends, and about as thick as a goose-quill, the male being 15 to 20 cm. (6 to 8 inches) long and the female much longer. It is characterized by a peculiar disagreeable odor. The eggs, which the female discharges in enormous numbers, are oval, 50 to 75 by 36 to 55 $\mu$, provided with a thick envelope, and as ordinarily passed in the stools contain no trace of embryos. They are very tenacious of life. It is generally believed that no intermediate host is required for the development of the parasite, although Stewart[1] states that it is necessary in the life cycle for the eggs to be swallowed by rats or mice, and that these animals transmit them after they have undergone certain developmental changes to man. Both Stewart and Ransom and Foster[2] have shown that the embryos which hatch out from the mature eggs in the alimentary canal do not at once settle down in the intestine, but migrate to the liver, spleen and lungs, and finally reach the alimentary tract again by way of the lungs, trachea and esophagus. On reaching the alimentary tract a second time they complete their development, if in a suitable host, or if in an unsuitable host, such as a rat or mouse, they pass out of the body in the feces. Man is infected by drinking polluted water or eating contaminated food. It is possible that flies may be a factor in disseminating the ova (Stiles). The mature parasite lives in the small intestine, but sometimes it ascends to the stomach and escapes by the mouth or nose, and rarely it wanders into the bile-ducts or enters the pancreas. Worms entering the common bile-duct may not only cause obstructive jaundice, but by carrying infective material from the intestine, may even set up suppurative inflammation of the ducts or liver. In very rare instances the parasite has invaded the larynx from the throat, causing asphyxiation, or has passed through the Eustachian tube into the middle ear. It is possible that in infants the passage of the larvæ through the lungs may sometimes be a cause of bronchopneumonia. Roundworms occasionally penetrate the intestinal wall and invade the peritoneal cavity, but it is doubtful whether they can do this in the absence of any mural lesion. As a rule, only a few worms are present in one case, but they may be very abundant. In rare instances they have formed a mass sufficiently large to cause intestinal obstruction. Recent studies indicate that some of the constitutional disturbances occasionally observed in ascariasis may be due to toxic substances elaborated by the parasite.

**Symptoms** may be entirely in abeyance, the worms being an accidental finding in the stools. In some cases, however, there are gastrointestinal symptoms, especially foul breath, capricious and variable appetite, abdominal discomfort, irregular movements of the bowels, flatulence, etc., as well as various nervous symptoms, such as headache, giddiness, grinding of the teeth in sleep, etc. In long-continued cases a general cachexia characterized by a pale or sallow skin, sunken eyes, and wasting may supervene. Eosinophilia is occasionally noted. In the comparatively rare cases in which ascarids wander into remote passages or organs the symptoms vary with the part visited and may be of great severity or may even terminate fatally. The *diagnosis* can be made with certainty only by finding the worms passed by the rectum or mouth or the ova in the stools.

[1] Brit. Med. Jour., 1912, ii, 5, 474, 486 and 753.
[2] Jour. Agric. Research, 1917, xi, 395.

**Treatment.**—Santonin is the most efficient remedy. It is best given at bedtime with calomel (2 to 5 gr.—0.13–0.3 gm.) and followed by a saline or cascara sagrada in the morning, if purgation does not occur on waking. The dose of santonin for a child of 2 years is ¼ to ½ grain (0.016–0.03 gm.), for a child of six years 1 grain (0.06 gm.), and for an adult 2 to 3 grains (0.13–0.2 gm.). The treatment should be repeated at intervals of 2 or 3 days as long as worms continue to be passed. Other useful remedies are oil of chenopodium (3 to 5 min.—0.2 –0.3 mil) on sugar or in capsules, three times a day, and fluid extract of spigelia (½ to 1 dr.—2.0–4.0 mils), three times daily. Thymol may also be used.

## OXYURIASIS

### (Pinworm Infection; Seatworm Infection)

Infection with *Oxyuris vermicularis* is widespread and is very common in children, although it is not rare in adults, especially women. The parasite is minute, fusiform, white, and, as its popular name implies, thread-like. The female is from 10 to 12 mm. (⅓ to ½ inch) in length, and has a long awl-shaped caudal extremity. The male is about half the length of the female and has a blunted tail end. The eggs, which are produced in great numbers, are oval, flattened on one side, and measure 50 by 20 μ. The embryo is often visible within the egg. Infection is direct, without an intermediate host, and occurs by the ingestion of eggs, which are passed out with the feces. The embryos escape from the eggs in the stomach or small intestine and then wander to the colon, rapidly reaching sexual maturity. The adult worms are most abundant, as a rule, in the cecum, which may contain an enormous number. The fertilized female migrates to the rectum, where she lays her eggs, or passes on to deposit then around the anus outside. The life cycle from the egg to sexual maturity is about 5 weeks. The eggs may find their way into the mouth from food, toys, soiled bed-clothing, etc. In some instances house-flies are probably carriers of the infection. Autoinfection is of common occurrence, patients in scratching about the anus to allay itching often taking up the eggs under the finger-nails and subsequently conveying them to the mouth.

**Symptoms.**—One symptom, at least, is usually present if the infection is at all heavy and that is intense itching about the anus, especially at night, due to the out-wandering of the female parasites. As a result of scratching, local hyperemia or even eczema sometimes ensues. The persistent discomfort disturbs sleep and in sensitive children may lead to various nervous disturbances, such as headache, picking at the nose, grinding of the teeth and crying out during sleep, and possibly convulsions. Incontinence of urine may also occur. Very heavy infections often cause more or less gastro-intestinal derangement, as well as proctitis, with tenesmus and mucous discharges. Masturbation may be induced by the irritation, and in girls leucorrhea sometimes results from the migration of the worms into the vagina. Occasionally the parasites invade the bladder, uterus and even the peritoneal cavity. The appendix not rarely contains them, and in some instances they appear to have been responsible for appendicitis.

**Treatment** consists in administering anthelmintics and cathartics by the mouth to dislodge the parasites that are in the small intestine and cecum and in using enemas to procure the expulsion of the gravid females from the rectum. By the mouth, santonin, spigelia or oil of chenopodium may be given, with cathartics, every two or three days, as mentioned in the treatment of ascariasis. Bismuth subcarbonate in large doses is sometimes efficacious.

The remedies most advantageously employed in enemas are decoction of quassia (1 oz. to 1 pint—30.0 gm. to 500 mils); lime-water, undiluted; sodium chloride (1 dr. to 1 pint—4.0 gm. to 500 mils); and tannin (½ dr. to 1 pint—2.0 gm. to 500 mils). To secure the best results the lower bowel should first be thoroughly emptied by means of a soap-and-water enema. The itching about the anus may be relieved by an ointment of boric acid, of metallic mercury or of one containing calomel, 20 gr. (1.3 gm.) and menthol, 5–15 gr. (0.6–1.0 gm.), to the ounce. Thorough and frequent cleansing of the body, bed-clothing, bedroom, and all articles handled by the patient is absolutely necessary to prevent reinfection by the eggs. Washing of the hands and buttocks after defecation is especially important. Temporary relief is readily obtained, but complete dislodgement of the parasites from the bowel is sometimes very difficult, especially in adults.

## TRICOCEPHALIASIS

### (Whipworm Infection)

Infection with *Trichuris* (*Trichocephalus*) *trichiura*, the whipworm, is widespread and common. The worm is small, thickened at one end and tapering like a whip-lash at the other. The male is about 40 mm. in length and the female is slightly longer. The parasites inhabit the cecum, but sometimes migrate to other parts of the intestinal tract. The eggs measure about 50 by 22 μ, and are of a yellowish-brown color, with a characteristic clear knob at each pole. Development is without an intermediate host and infection is acquired from food or drink, contaminated with the eggs. *Symptoms* are usually absent, but in some cases a more or less pronounced anemia supervenes. In a few instances whipworms seem to have been the exciting cause of appendicitis. The *diagnosis* is made by finding the worms or the characteristic eggs in the stools.

**Treatment** is unsatisfactory. Thymol and male-fern are the drugs usually advised.

## STRONGYLOIDOSIS

Infection with *Strongyloides stercoralis* occurs especially in tropical and subtropical countries, but cases have been reported from almost every part of the world. The parasitic adult worms (2 to 3 mm. long), which are probably parthenogenetic females, live in the intestinal canal, where they produce numerous ova, which hatch out before leaving the bowel, appearing in the feces as rhabditiform embryos. The latter, which are transparent, actively motile parasites, about 0.3 mm. long by 0.02 mm. broad, with a blunt head and a pointed tail, may develop directly into filiform embryos or into free-living sexually differentiated adults. From the eggs of the latter are produced rhabditiform embryos, which in turn undergo transformation into the filiform stage. The filiform embryo enters man through the mouth or skin, and in the intestine develops into the parthenogenetic mother worm. The parasite may prove harmless, or it may set up intestinal catarrh and diarrhea, which is usually unaccompanied by pain or fever. The diagnosis is made by finding the rhabditiform embryos in the stools. The *treatment* is that of catarrhal enteritis, with the administration of thymol at intervals, as in uncinariasis.

## UNCINARIASIS, ANKYLOSTOMIASIS, OR HOOKWORM DISEASE

Hookworm disease occurs in virtually all tropical and subtropical countries, and in many of these, especially in the rural districts, from 40 to 90 per

cent. of the inhabitants are infected. Even in more temperate regions it is by no means uncommon among miners and others who frequently come in contact with wet soil. In the southern states of the United States and in the West Indies the disease is very prevalent. The poor suffer much more than the well-to-do.

There are two species of parasites: *Ankylostoma duodenale* (*Uncinaria duodenalis*) and *Necator americanus* (*Uncinaria americana*) which closely resemble each other, although they differ in certain minor respects. The male is from 10 to 12 mm. (⅓ to ½ inch) in length and about 0.4 mm. (1/60 inch) in breadth. The female is somewhat larger. The eggs, which are very abundant, are oval, thin shelled, and almost colorless. They measure about 60 μ by 40 μ. The parasites inhabit the small intestine, especially the jejunum and ileum. The eggs are passed in large numbers with the feces and if these are deposited on the ground and exposed to the air in a warm, damp and shaded place larvæ soon hatch out and in the course of a week or ten days reach an infecting stage. Under favorable conditions of warmth and moisture the larvæ may remain alive for at least several months, but unless they gain entrance into the intestine of a human being they cannot attain sexual maturity.

The laval parasites may pass directly into the digestive tract with contaminated food or water or with dirt on the hands, although usually, as Looss[1] first demonstrated, infection takes place indirectly by way of the skin, the route being from the blood to the heart, from the heart to the lungs, from the lungs to the larynx, and thence to the esophagus, stomach and bowel. The entrance of the larvæ through the skin, usually that of the feet or legs, is followed by a transitory erythematopapular eruption, known as "Ground Itch" or "Mazamorra." By the end of 6 or 8 weeks after infection occurs ova begin to appear in the stools. It has been shown that the uncinariæ, which sometimes are present in great numbers, may live in the intestine as long as 12 years (Wells), consuming the blood of the patient, biting the intestine and causing occult hemorrhages, and probably producing a toxin with hemolytic properties (Preti,[2] Bondonoy,[3] Schwartz.[4])

**Symptoms.**—Infected persons, although a source of danger to others, do not always present noteworthy symptoms. Many cases, however, are characterized by gastrointestinal disturbances, fugitive abdominal pains, indisposition to exertion, a low intermittent fever, and later by a more or less pronounced secondary anemia, with eosinophilia. Physical and mental lethargy is, as a rule, a conspicuous feature, and in the severe and advanced cases the clinical picture is one of extreme anemia, with pallor of the skin and mucous membranes, edema, throbbing of the vessels, difficulty in breathing, etc. The hemoglobin is usually reduced in greater proportion than the number of erythrocytes, the leucocyte count is normal or slightly less than normal, and unless the resistance is poor, the percentage of eosinophiles is high, averaging about 8 or 10. Retardation of development, sometimes amounting to actual infantilism, is by no means rare in cases occurring before puberty. A definite *diagnosis* is based on finding the eggs or the worms in the feces, and these should be carefully examined in every suspected case. A simple and very satisfactory method is that of Kofoid and Barber,[5] which consists in stirring a portion of feces in a test-tube with hypertonic saline solution and allowing the mixture to stand until the debris sinks. The ova

[1] Cent. f. Bakt. u. Infectionsk., 1903, 1904.
[2] Münch. med. Woch., 1908, lv, 436.
[3] Arch. Parasitol., 1910, xiv, 5.
[4] Arch. Int. Med., 1920, xxvi, 431.
[5] Jour. Amer. Med. Assoc., 1918, lxxi, 1557.

float near the surface. The *prognosis* is good, under appropriate treatment, even in severe cases.

**Treatment.**—The most efficient remedies are oil of chenopodium and thymol. On the day previous to the administration of the anthelmintic, the patient should have only liquid food and in the afternoon of that day he should be given a full dose of magnesium sulphate. On the following morning, while fasting, he should be given 12 minims (0.75 mil) of oil of chenopodium, in freshly filled hard capsules, twice, with a two-hour interval, or two 30-grain (2.0 gm.) doses of thymol, triturated with equal parts of milk-sugar, with a two-hour interval. An hour after the last dose of the anthelmintic the purge of magnesium sulphate should be repeated. The patient should remain in bed during treatment and no food should be taken until after the bowels have moved thoroughly, and even then, if thymol has been used, alcoholic drinks, oils, milk and greasy foods must be withheld as they all are solvents of the drug. Several courses of treatment, given at weekly intervals, are usually necessary for cure. In refractory cases Kantor's[1] method of introducing a concentrated dose of the vermifuge directly into the intestine through a tube may be employed with advantage.

Important factors in prophylaxis are thorough treatment of all infected persons, the abolition of promiscuous defecation, especially defection on the surface of the ground, proper protection of the feet and legs, cleanliness of the hands, care in the preparation of fruits and vegetables that are eaten raw and the avoidance of water that may be infected.

## TRICHINIASIS

(Trichinosis)

Trichiniasis, or infection with *Trichinella spiralis*, is widespread, outbreaks or sporadic cases occurring from time to time wherever pork forms an important article of diet. As a sporadic disease it is doubtless more common than is usually supposed. The method of infection is by the ingestion of raw or insufficiently cooked trichinous pork, which upon entering the alimentary canal is freed of its larvæ, the surrounding cysts being destroyed by the digestive juices. In the intestines the larvæ develop into sexually mature worms, which are from 1½ to 4 mm. long. The male worm soon dies but the female survives to give birth to hundreds of active embryos, which find their way through the intestinal wall into blood- or lymph-streams, and in about ten days or two weeks after infection lodge in the voluntary muscles, where they set up a myositis, coil themselves up and become encapsulated, and finally undergo retrogressive changes, an event which in many cases is preceded by calcification of the capsules. The encysted larvæ ("fleshworms") may remain alive in the muscles for many years. The cysts are elliptical, about ½ mm. in length, and, when calcified, visible with the naked eye as minute grayish-white specks. Hogs become infected by eating scraps of raw pork or rats containing the encysted parasites, and rats by eating scraps of raw pork or other rats that are trichinous. Fifty thousand trichinæ and upward may be present in a single ounce of pork.

**Symptoms.**—After pork containing the live larvæ is eaten there is a period of incubation lasting from several hours to several days, and this is followed by gastro-enteric symptoms, consisting of anorexia, nausea or vomiting, abdominal pains, and, frequently, profuse diarrhea. Fever is an early feature. It may be remittent or intermittent, and usually lasts from a few days to 3 or 4 weeks. Occasionally the temperature reaches 104° or 105° F. The fever is accompanied, as a rule, by vague muscular pains,

[1] Jour. Amer. Med. Assoc., 1919, lxxiii, 1181.

general malaise and mental hebetude. In the course of about 10 days muscular symptoms become conspicuous. Movements cause pain and the muscles themselves are tender and often somewhat swollen and tense. If the intercostal muscles and diaphragm are especially affected there may be pronounced dyspnea, and if the laryngeal muscles are invaded there may be hoarseness or aphonia. With the muscular soreness there is frequently profuse sweating. Edema of the face, especially of the eyelids, is observed in a large proportion of cases. It usually lasts but a few days, although in some instances it recurs at a later period. Examination of the blood generally shows a moderate leucocytosis and almost invariably a pronounced eosinophila (25 to 50 per cent. or more). In the early stages the parasites themselves may sometimes be demonstrated in the blood,[1] and also in the cerebrospinal fluid. Occasional symptoms are pruritus, a papular or vesicular eruption, subconjunctival ecchymoses, and stiffness of the neck and other signs of meningeal irritation. In very severe infestation delirium and somnolence may develop, there may be extreme emaciation, and finally death may occur from exhaustion. On the other hand, in light cases slight muscular soreness may be about the only manifestation. With the encapsulation of the larvæ the symptoms gradually subside, the average duration of the active phase of the infection being about 3 or 4 weeks. Occasionally several months elapse before recovery is complete. Except in very severe infections the outlook is good, the average mortality not being over 5 per cent. The prognosis is better in children than in adults.

Trichiniasis may often be suspected by the occurrence of muscular soreness, swelling of the eyelids and fever after an attack of acute gastro-intestinal catarrh. If there is also eosinophilia the evidence may be regarded as almost conclusive. A positive diagnosis, however, is made by finding the larvæ in the cerebrospinal fluid, in the blood, or in a bit of muscle excised from the calf of the leg or the deltoid, under cocain anesthesia, teased out in glycerin and examined under low power. Simple myositis and typhoid fever may resemble trichinasis more or less closely, but with ordinary care they should be readily excluded.

The best **preventive** of infection is thorough cooking or curing of all pork before it is eaten. According to Ranson and Schwartz[2] larvæ of Trichina spiralis are quickly destroyed by exposure to a temperature of 131° F. (55° C.), gradually attained. Meat inspection under government supervision has not yielded entirely satisfactory results. With regard to **treatment,** if the infection is recent lavage of the stomach and active purgation are indicated. Santonin might prove of service. Otherwise the treatment is symptomatic. Hot applications or hot baths and morphin may be required to relieve pain and stimulants to combat exhaustion.

## FILARIASIS

Filariasis, or infection with threadworms of the genus Filaria, is more or less common in most tropical and subtropical countries, whence it is occasionally carried to temperate regions. It is especially prevalent on the west coast of Africa, in South China, certain islands of the Pacific Ocean (Philippines, Samao, Fiji), and the West Indies. Although several species of filaria are parasitic in man, interest centers chiefly around *Filaria bancrofti.* The adult parasite, which occurs only in human beings, has the appearance of a slender white thread from 4 to 10 centimeters (1½ to 4 inches) long.

[1] The best method of examination is that for Filaria; see page 316.

[2] Jour. Agric. Res., Aug. 15, 1919.

After the death of the host the worms are usually found in the lymphatics. The larval forms (microfilariæ) occur in a number of mosquitoes (*Stegomyia pseudoscutellaris, Culex quinquefasciatus, Mansonia uniformis,* etc.) and also in the circulating blood of infected human beings. In fresh human blood the parasite appears as a minute snake-like organism, wriggling actively and displacing the corpuscles, but changing its location on the slide little, if any. It is about 0.3 mm. ($\frac{1}{100}$ inch) in length, blunt at one end and sharply pointed at the other, and enveloped in a delicate sheath or vitelline membrane. The number that may be seen in a single drop of blood varies from one to several hundred. In many cases the parasites can be found in the blood only during sleeping hours.

Man is infected through the bite of a mosquito which has swallowed the larvæ while biting a patient. The larvæ after reaching a certain development in the muscles of the mosquito pass into the salivary system of the insect, whence they are again injected into the blood of man. In the human host the filariæ attain maturity and find a resting place in the lymphatic system, especially of the abdominal cavity, scrotum and testes. In these locations the female produces embryonic or larval forms (microfilariæ), which soon escape into the peripheral blood by way of the thoracic duct.

**Effects.**—The microfilariæ in the blood apparently cause no disturbance, and in many cases even the adult parasites fail to produce serious results. Ill effects depend upon blocking of the lymph-channels and vary with the site of the obstruction and the character and degree of the secondary changes. When the thoracic duct is occluded the increased lymph pressure results in varicosity of the lymphatics or edema, or both. In some cases the lymph-vessels of the urinary tract rupture in consequence of the strain to which they are subjected and *chyluria* or *hematochyluria* supervenes. At times the worms by damaging the tissues allow an ingress of pyogenic bacteria, which in turn set up purulent foci (*filarial abscesses*). Perhaps the most frequent manifestation of filarial infection is *elephantiasis* (Elephantiasis arabum, Barbadoes leg). This condition, which usually affects one or both of the lower extremities, alone or with the scrotum, begins with attacks of lymphangitis and erysipelatoid inflammation. The exudation is only partially absorbed, and each successive attack leaves the tissue more swollen and hyperplastic, so that in advanced cases the affected part is enormously enlarged and the skin over it is thickened, fibrous, and adherent to the underlying structures. It is generally held that the blocking of the lymph-channels upon which elephantiasis depends is caused partly by the premature discharge of ova, in consequence of an injury to the female parasite, and partly by recurrent lymphangitis, for which secondary bacterial infection is responsible. In elephantiasis of the scrotum—so-called *lymph-scrotum*—a tumor weighing from 10 to 50 pounds or more is frequently developed. With the occurrence of elephantiasis of the legs, the microfilariæ usually disappear from the blood, probably because the channels by which they would reach the blood-stream are blocked. Eosinophilia, averaging about 10 per cent., is the rule in filarial infections.

The **diagnosis** of filariasis is made by detecting the larvæ in the blood. The Smith-Rivas method yields good results in doubtful cases. It consists in adding 1 mil of blood to 10 mils of a 2 per cent. acetic acid solution and examining the sediment obtained by centrifugalizing the mixture.

**Medical treatment** is very unsatisfactory, although good results have been ascribed to the use of thymol, ichthyol, methylene blue, and arsphenamin. Surgical intervention is sometimes indicated. Spontaneous arrest of the disease often occurs. Prophylactic measures include the extermination

of mosquitoes, the prevention of infection of mosquitoes, and the prevention of infection by mosquitoes.

**Filaria loa** has the peculiar property of migrating freely through the tissues, causing at times itching or other parasthesiæ and more rarely fleeting tumefactions (Calabar swellings) in different parts of the body, especially around the eye. The larvæ are found in the blood chiefly during the day time. According to Leiper[1] the intermediate host is a fly of the genus *Chrysopa*.

## DRACUNCULOSIS

(Dracontiasis; Guinea-worm Infection)

Infection with *Dracunculosis medinensis*, the Guinea-worm, is widespread in Asia and in certain parts of Africa, and imported cases occasionally appear in the United States and South America. The adult worm is from 60 to 80 or more cm. (2 to 3 feet) long and about 1.5 mm. $\frac{1}{15}$( in.) in diameter. The embryo may live in water for 2 or 3 weeks, and if ingested by a minute crustacean (Cyclops) is transformed into a larval stage, which may gain access to man through drinking water. In man the female worm after reaching maturity (10 to 15 months) migrates to the subcutaneous tissue, usually of the leg or foot, and there gives rise to a painful vesiculopustular lesion, which in a few days ruptures, leaving an ulcer at the base of which the head of the parasite may be seen. In the course of a week or two the worm and its young are extruded, and the ulcer gradually heals. If the worm is ruptured by clumsy attempts at extraction, however, and the embryos are discharged in the tissues, an abscess results, which may be followed by general septicemia. As a rule, only one worm is present in the body at one time, although exceptionally there may be two or more. **Treatment** consists in excising the worm while alive or injecting into it chloroform or a 1:1000 solution of mercuric chlorid.

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## DISTOMATOSIS

(Distomiasis; Trematode Infections; Fluke Infections)

As a human disease, distomatosis, or infection with flukes, is comparatively rare in the United States and Continental Europe, but it is endemic in certain parts of Asia, Africa and South America. The adult parasites are small organisms with soft, flattened, leaf-shaped bodies. They are smooth or covered with minute spines, and possess a mouth and one or two suckers. The largest species attains a length of about 40 mm. (1½ in.) and a breadth of 12 mm. (½ inch). With the exception of the blood-flukes, all trematodes are hermaphroditic. The ova develop into ciliated, free-swimming embryos, which in most cases require an intermediate host before reaching maturity in man.

The important clinical forms of distomatosis are pulmonary, hepatic, intestinal and hemic distomatosis.

**Pulmonary Distomatosis (Paragonimiasis, Parasitic Hemoptysis).**—This is caused by *Paragonimus westermanii* and prevails especially in China, Japan, Formosa and Korea. It is thought that the intermediate host is a snail and that man is infected through contaminated water or food. The

[1] Brit. Med. Jour., Jan. 4, 1913.

parasite is found in the lungs in small superficial cavities, which communicate with the bronchi and which contain also numerous ova and a reddish slimy fluid. The chief *symptoms* are cough, reddish-brown expectoration and more or less severe hemoptysis. In advanced cases the condition so closely resembles pulmonary tuberculosis that it can be differentiated only by finding the characteristic eggs in the sputum. Occasionally the brain, liver, eyelids, etc., become involved. There is no specific *treatment.* Disinfection of the sputum, general hygienic measures and change of residence are the important indications.

**Hepatic Distomatosis.**—Several species of flukes have been found in the liver of man, but the most important is *Opisthorchis sinensis* (*Distoma sinense*), which occurs extensively in Japan, China, and India. A number of imported cases have been found in the United States. Man is probably infected directly from water or indirectly from raw fish or snails. *Fasciola hepatica* and *Dicrocœlium lanceatum* (lancet fluke), which are of common occurrence in sheep and cattle, are rare and accidental parasites in man.

Adult liver-flukes inhabit the bile-ducts and produce pathologically dilatation of the ducts, cholangitis and various degrees of cirrhosis. *Clinically,* they may cause painful enlargement of the liver, diarrhea, jaundice and intermittent ascites. Death may be due to exhaustion from diarrhea, etc., or to suppurative cholangitis. The *diagnosis* is made by the discovery of the ova in the stools.

**Intestinal Distomatosis.**—Of the several flukes that may invade the intestines, the most important is *Fasciolopsis Buski,* which is of Asiatic origin. Neither the life-history of the parasite nor the source of infection is definitely known. The chief *symptoms* of intestinal distomatosis are said to be various digestive disturbances and diarrhea with bloody stools. Thymol and calomel are claimed to be effective remedies.

**Hemic Distomatosis (Bilharziosis, Schistosomiasis).**—This infection is due to *Schistosoma hæmatobium,* described by Bilharz in 1852, and occurring chiefly in Africa, to *Schistosoma japonicum,* prevailing especially in Japan, China and the Philippines, and to *Schistosoma mansoni* occurring in the West Indies and South America. The parasites, which are bisexual, are found most frequently in the portal vein and its branches, although the copulating adults seem to show a predilection for the veins of the bladder and rectum. The ova bore through the tissues and finally escape from the body with the urine or feces. In water they rapidly hatch out into ciliated larvæ (miracidia), which gaining access to certain molluscs develop into infecting forms (cercariæ). The channel of infection is not definitely known, but the weight of evidence favors the view that the parasites enter the body directly through the skin while a person is bathing in a contaminated stream. Bilharziosis affects especially the poorer classes and is much more common in males than in females. A very large proportion of the male population in Egypt and in certain parts of South Africa is said to be infested.

The *lesions* in the bladder and rectum are produced mainly by the ova and consist of chronic inflammatory changes, fibroid thickening and polypoid excrescences (bilharzian tumors), which clinically may readily be mistaken for malignant growths. *Symptoms* may be entirely in obeyance. When present, they vary according as the bladder or the rectum is chiefly involved. In vesical schistosomiasis (endemic hematuria) the salient features are usually hematuria, vesical tenesmus and pain in the back and perineum. Various complications, however, such as cystitis, pyelonephritis, urinary fistula, vesical or renal calculus and bilharzian tumor of the bladder or vagina, are likely to arise. Rectal schistosomiasis is characterized by diarrhea with

bloody stools, and, as the disease advances, recurrent fever and enlargement of the liver and spleen. Japanese schistosomiasis begins with febrile symptoms, urticarial outbreaks and pulmonary manifestations suggesting bronchopneumonia; later, the stools become mucous and bloody, and finally cirrhosis of the liver with ascites supervenes. Eosinophilia is commonly present in all forms of schistosomiasis and many patients becomes anemic, emaciated and exhausted as a result of bleeding and suffering. The *diagnosis* is based upon finding the ova in the urine or feces or in shreds obtained from the bladder or rectum. As to life, the prognosis is fairly good, but as to health, unfavorable. Not rarely, however, the infection eventually dies out.

*Prophylaxis* consists in guarding the water from the urine and feces of patients with the disease and in avoiding impure water not only for drinking, but also for bathing. Until recently the *treatment* has been mainly symptomatic. Good results are claimed for hexamethylenamin and methylene blue in vesical infection and for santonin and aspidium in rectal infection. Recently excellent results have been reported from intravenous injections of tartar emetic, given on alternate days, in doses gradually increased from ¼ grain (0.016 gm.) to 2 grains (0.13 gm.), the treatment being continued for about a month or until from 15 to 20 grains (1.0–1.3 gm.) of the drug have been taken. The best vehicle is normal saline solution, from 2 to 10 mils being used according to the dose of tartar emetic. Cawston,[1] has obtained good results from intramuscular injections of emetin hydrochlorid, daily for three days and then three times a week for three weeks, commencing with a grain (0.06 gm.) and gradually increasing the dose to 2 grains (0.13 gm.).

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## ACARIASIS

The acarines, which include ticks and mites, may produce disease directly or they may act as intermediate hosts of other parasites and produce it indirectly.

**Ixodiasis (Tick Infection).**—Of the many ticks that are known to attack man the most important are *Ornithodorus moubata*, the agent active in transmitting the Spirochæta duttoni, the cause of African relapsing fever, or tick fever, and *Dermacentor venustus*, the agent active in transmitting the virus of Rocky Mountain fever.

Temple,[2] Todd,[3] Strickland,[4] McCornack,[5] and others have reported cases of acute, progressive motor paralysis of the flaccid type in man, usually children, as a result of ticks (D.venustus) imbedded in the scalp, the external ear, the axilla or other protected parts. Death sometimes occurred, but, as a rule, removal of the tick was followed by a rapid recovery.

**Sarcoptic Acariasis (Scabies).**—Infection with *Sarcoptes scabei*, the itch mite, is widespread. The female parasite, which is just visible to the unaided eye, measures 0.33 to 0.45 by 0.25 to 0.35 mm., and the male is somewhat smaller. The male lives on the surface, but the female burrows into the epidermis causing intense itching, which leads to scratching and an eruption of papules, vesicles and pustules. Almost any part of the body may be attacked, but the favorite sites are the interdigital spaces, the flexures of the

[1] Lancet, Nov. 19, 1921.
[2] Med. Sentinel, 1912, v, 507.
[3] Canadian M. A. J., 1919, ix, 994.
[4] Parasitology, 1914, vii, 379.
[5] Jour. Amer. Med. Assoc., 1921, No. 4, 260.

wrists, the axillary folds, the penis in males and the mammæ in females. The peculiar distribution of the lesions and the presence of the burrows or tracks produced by the female mites are the diagnostic features. The burrows are straight or zigzag, dotted, grayish or brownish thread-like elevations, measuring from 1 to 4 or 5 mm. in length. The disease is acquired by close contact with infected persons or with articles containing the itch mites. The *treatment* consists in thoroughly cleansing the entire body with green soap and hot water, and then rubbing in twice a day for four days an ointment of sulphur—1 dram (4.0 gm.) to the ounce (30.0 gm.). At the end of this time another bath should be taken and the underclothing and bed linen changed and sterilized.

Among other mites are *Demodex folliculorum*, which is found in the sebaceous glands and which is usually considered to be harmless, and *Pediculoides ventricosus*, which is found in the dust of straw or grain, and which is the cause of "straw itch."

## PARASITIC INSECTS

**Pediculosis (Lousiness).**—Three specimens of lice attack man. *Pediculus humanus* (*capitis*), the head louse; *Pediculus corporis* (*vestimenti*) the body louse; and *Phthirius pubis* (*Pediculus pubis*), the pubic louse or crab louse. They cause itching, which excites scratching and leads to excoriations and eczema. The louse, especially *Pediculus corporis*, is the agent concerned in the transmission of typhus fever, trench fever, and of North African and Indian relapsing fevers. The *treatment* for headlice consists in cutting the hair and applying to the head kerosene oil, tincture of cocculus indicus, or, if there is much pustulation, an ointment of ammoniated mercury—20 to 30 grains (1.3–2.0 gm.) to the ounce (30.0 gm.) The essential measure in the treatment of body lice is sterilization of the clothes and bed linen. These should be thoroughly boiled, baked, or soaked in a 5 per cent. compound cresol solution for an hour. In treating for pubic lice the parts should be thoroughly cleansed and then anointed with ammoniated mercury ointment—40 gr. (2.6 gm.) to the ounce (30.0 gm.) of petrolatum.

**Fleas.**—There are two species of jumping fleas in particular that attack man: *Pulex irritans*, the common or house flea, and *Ctenocephalus canis*, the cat and dog flea. Fleas may act as ectoparasites, biting man; as intermediate host for certain tapeworms (double-pored dog-tapeworm); and as disseminators of plague (rat flea). Fumigation with sulphur, sprinkling about pyrethrum powder, and washing the woodwork with hot soapsuds are the measures recommended for ridding houses of fleas.

The burrowing flea, jigger flea, or chigger (*Sarcopsylla penetrans*), is common in tropical and subtropical countries. The impregnated female penetrates the skin, usually of the feet, giving rise to painful edema, pustulation and, at times, ulceration.

*Treatment* consists in removing the flea with a blunt needle after having killed it by applying chloroform.

**Bedbugs.**—The common bedbug, *Cimex lectularius*, preys upon the skin, sucking the blood and producing by its bite a wheal with a central hemorrhagic point. Bedbugs have been suggested as possible transmitting agents of European relapsing fever and septicemic plague. To rid houses of the insects Stiles recommends fumigation with sulphur (2 pounds to 1000 cubic

feet of space). The floor and woodwork generally should be washed with mercuric chlorid solution (1 to 5000).

**Myiasis.**—This term is applied to infection with the larvæ of various species of dipterous insects, especially flies. The best known of the myiases is that caused by the larvæ of the *bot-fly* (*Oestrus*), which is common in the tropics. The ova are deposited in the puncture made by the insect in the skin, and in developing give rise to a painful furuncular swelling. A blue-bottle fly, *Compsomyia macellaria*, may lay its eggs in wounds or in orifices having fetid discharges, such as those of the nose or ears, and the larvæ, which issue within a few hours, may burrow into the tissue and cause frightful ravages. Irrigation with a 5 per cent. solution of phenol is the best *treatment*.

In tropical countries various intestinal disturbances may also be caused by dipterous larvæ which have gained access to the intestinal tract in food.

# INTOXICATIONS

## ALCOHOLISM

Alcoholism is an acute or chronic condition resulting from the immoderate use of alcoholic beverages.

### ACUTE ALCOHOLISM

The ingestion of a large quantity of alcohol first causes apparent stimulation, with flushing of the face, quickened breathing and pulse, motor restlessness, impulsiveness, exaggerated talkativeness, a sense of well-being, and a deceptive feeling of increased strength and capability. Within an hour, or in much shorter time if a very large dose has been taken on an empty stomach or if the person has not been accustomed to the use of alcohol, the functions of the central nervous system become definitely depressed, as shown by mental confusion, thick muttering speech, uncertain gait, general muscular relaxation and drowsiness. In some cases before the occurrence of sopor the abolition of emotional restraint results in maniacal excitement, but usually the patient is only merry and silly. Retching and vomiting may also occur. Gradually the drowsiness deepens into sleep, and then, if the intoxication is sufficiently severe, coma and symptoms of medullary depression supervene, this stage being characterized by dilatation of the pupils, slow and stertorous breathing, feeble pulse, clammy skin, subnormal temperature, abolition of most of the reflexes and sometimes relaxation of the sphincters. Occasionally, the coma is interrupted by convulsions.

Recovery is the rule, but death may occur within a few hours from respiratory paralysis, cardiac failure, or pulmonary edema. With the return of consciousness symptoms of gastric irritation—anorexia, coated tongue, nausea and vomiting—develop, with depression, headache, and general muscular soreness ("Katzenjammer"). Alcoholic coma must be distinguished from coma due to apoplexy, uremia, diabetes, cranial injuries, epilepsy, thermic fever, opium poisoning, etc.

**Treatment.**—The stomach should be emptied by the stomach-pump or a hypodermic injection of apomorphin (1/8 gr.—0.008 gm.). Catheterization may be required. In case of threatened collapse recourse must be had to external heat, enemas of hot saline solution, and subcutaneous injections of caffein, strychnin and atropin. The subsequent headache, nervousness and gastric irritability are best relieved by a laxative dose of calomel, with the administration of sodium bicarbonate and bismuth subcarbonate before meals, and a bromid with caffein or a bromid with acetphenetidin after meals.

### CHRONIC ALCOHOLISM

The effects of the habitual use of alcohol in excess are due in part to the irritant action of the intoxicant and in part to its specific action on the nervous system. It is not unlikely, however, that some of the changes occurring in the viscera depend less upon the alcohol itself than upon secondary toxic products resulting from indigestion and faulty metabolism. The lesions in the alimentary canal are of an inflammatory character, while

those in the liver, kidneys, heart, muscles and nerves are essentially degenerative.

The most common manifestations of chronic alcoholism are injection of the conjunctivæ, redness of the face, particularly of the nose, the usual phenomena of chronic gastro-enteritis, tremor of the fingers, tongue and lips, muscular weakness, dulling of the mental faculties and deterioration of the morals. The general nutrition is often disturbed, some patients becoming more or less emaciated, others obese. Enlargement of the liver, in consequence of fatty changes, is a common occurrence and in some cases (5 to 6 per cent. of alcoholics), especially in spirit-drinkers, symptoms of atrophic cirrhosis of the liver eventually develop. In many instances the kidneys become the seat of cirrhotic and catarrhal changes. The ocurrence of arteriosclerosis and of chronic myocardial disease seems also to be favored by chronic alcoholism. A marked hypertrophy of the heart is not rarely seen in men who consume large quantities of beer and do very heavy work. Amblyopia due to orbital optic neuritis sometimes develops.

Of the nervous affections resulting from chronic alcoholism, polyneuritis is especially frequent; indeed alcoholism is the commonest cause of the toxic form of this disease. Proportionately more women are affected than men. In many cases the neuritic features are accompanied by a peculiar mental disturbance characterized by a loss of memory for recent events, lack of power of attention, fabrications, and disorientation as regards time and place (Korsakow's[1] psychosis). The outcome in most cases is favorable, but permanent dementia may supervene. Not rarely the prolonged use of alcohol leads gradually to definite insanity. This may manifest itself by simple progressive weakening of the mind, with episodic and transitory hallucinations and delusions, or it may take the form of a maniacal psychosis or of a paranoid dementia with more or less systematized delusions of a depressive or persecutory character. The lesions found most frequently in association with alcoholic insanity are hemorrhagic pachymeningitis, chronic leptomeningitis, and serous effusion into the ventricles. Microscopic examination reveals degenerative changes in the cortical cells and fibers.

Epileptic convulsions occasionally occur in the course of alcoholic psychoses or as isolated phenomena.

**Effect of Chronic Alcoholism on Offspring.**—Statistics indicate a much larger proportion of cases of deficient vitality, insanity, epilepsy, criminality and alcoholism among the children of alcoholics than among the descendents of total abstainers, but it is not definitely known whether the danger of alcoholic parents lies in the effect of the alcohol itself upon the germ-plasm or the fetal blood, or whether it lies in the transmission of the hereditary degeneracy which led to the inebriety of the parent or parents. Drunkenness in several generations of the same family may be the result of several factors, and it goes on until regression to the normal by conjugation with a healthy stock occurs, or terminates by degeneration and elimination of the stock (Mott[2]).

**Treatment of Chronic Alcoholism.**—The patient is best treated in a special hospital or sanatorium, as he rarely has sufficient will power of his own to abstain from drink. The alcohol should be withdrawn as rapidly as possible, usually within two or three days. Highly seasoned nutritious food should be given at frequent intervals. Robust patients are often benefited by warm baths (103° F.), for ten or fifteen minutes, followed by cold sponging.

[1] Arch. f. Psych., 1892, Bd. xxi, 669.
[2] Brit. Med. Jour., Oct. 28, 1905.

Cathartics are almost always indicated and should be given freely. Violent outbreaks the result of acute intoxication may often be subdued by a hypodermic injection of apomorphin, which has a sedative as well as an emetic action. Stomachics, such as nux vomica, capsicum and ginger, are frequently of service when given with food. Atropin hypodermically (1/120 gr.—0.0005 gm.), two or three times a day, is sometimes useful in controlling nervousness. Intramuscular injections of ergot have also been highly recommended. Sleep is best procured by chloral (15–20 gr.—1.0–1.3 gm.), paraldehyd (1 dram, 15.0 mils), repeated every hour, if necessary, for two or three doses, or scopolamin hydrobromid (1/100 gr.—0.00065 gm.). The mixture of morphin, 1/8 gr. (0.008 gm.); chloral, 20 grains (1.3 gm.); tincture of hyoscyamus, 1/2 dram (2.0 mils); tincture of capsicum 3 minims (0.02 mil); and water 1/2 ounce (15 mils), recommended by Lambert, is often effective. Strong moral support, the creation of suitable surroundings, mental diversion, abundant exercise in the open air, and a varied diet of wholesome food are the most effective means of keeping the patient from the use of alcohol. The prospects of permanent cure are better than with morphin or cocain. Relapse, however, is extremely common.

## DELIRIUM TREMENS

### (Mania à Potu)

Delirium tremens is an acute psychosis occurring in the course of chronic alcoholism. It is observed chiefly in drinkers of distilled spirits. The exciting cause is often found in the sudden withdrawal of alcohol, a debauch, abstinence from food, overexertion, psychic shock, trauma, a surgical operation or an acute infection, especially pneumonia. The pathogenesis of the condition is not known. Cerebral edema is often found at necropsy, but apparently this is a late or secondary feature.

Two well-defined stages of delirium tremens may be recognized: a premonitory stage, characterized by insomnia, restlessness, tremors, apprehensiveness and occasionally poorly-formed hallucinations; and a second stage characterized by widespread tremor, persistent insomnia, talkative delirium, and definite hallucinations of a terrifying character, usually of sight, but sometimes of hearing. The pulse is rapid and often weak, the skin is moist, the face is usually flushed, but it may be pale, and the temperature, even in the absence of pneumonia, is not rarely elevated a degree or two. In many cases, under appropriate treatment, the process does not continue beyond the premonitory stage, but terminates favorably in the course of two or three days. The second stage lasts, as a rule, two or three days and ends in recovery or in death. Convalescence often follows a prolonged sleep. In about ten per cent. of the cases stupor succeeds the delirium and symptoms of the so-called typhoid state supervene. Meningitic phenomena, such as general hyperesthesia, rigidity of the neck, exaggeration of the deep reflexes, etc., may also develop. This condition, which has been shown to be associated with an excessive accumulation of serous fluid in the pia-arachnoid space ("wet brain"), may persist for several weeks.

The mortality in delirium tremens varies with the stage during which treatment is instituted and the presence or absence of complications. It averages about 10 per cent., and after the occurrence of well-defined hallucinations it is not less than 25 or 30 per cent. In cases advanced to the stage of cerebral edema the mortality is about 80 per cent. Death is usually due to pneumonia, but it may be the result of a primary cardiac failure.

**Treatment.**—In the first stage the important indications are to support the system by means of nourishing food, to favor elimination through the administration of a quickly acting cathartic and the free use of water, and to secure sleep by giving bromids in doses of 1 dram (4.0 gm.) every three or four hours or of trional in doses of 20 grains (1.3 gm.), in hot milk or broth, every fourth hour, care being exercised not to overdo the exhibition of narcotics. Alcohol in moderate doses is undoubtedly of value at this period, although many writers recommend its withdrawal from the first. Cool packs in asthenic cases and warm baths in asthenic cases are helpful. Spinal drainage is sometimes of service, but, as a rule, it is more effective in the second stage.

In the second stage rest in bed is essential. Physical restraint is almost always required and may be secured by folded sheets drawn across the body and tied to the bed and by the use of wrist- and ankle-straps. An abundance of nourishment in the form of milk, milk and eggs, and highly seasoned broths, with eggs beaten into them just as they have ceased boiling, is necessary. In uncomplicated cases alcohol is better avoided in this stage. Somnifacients are much less effective than in incipient cases, but bromids, chloral, paraldehyd or trional should be used. Morphin should be given sparingly, if at all. Lambert speaks favorably of a combination of strychnin ($\frac{1}{30}$ grain—0.002 gm.), hyoscin sulphate ($\frac{1}{100}$ grain—0.0006 gm.), and apomorphin hydrochlorid ($\frac{1}{10}$ grain—0.006 gm.). In robust patients cold effusions, followed by vigorous rubbing, are sometimes of aid in producing sleep. Spinal drainage is often advisable. For circulatory weakness the most efficient remedies are digitalis, strychnin and atropin.

Alcoholic wet brain is best treated by giving highly nutritious liquids, using the nasal tube, if necessary; by securing free evacuation of the bowels; by administering circulatory stimulants (digitalis, caffein, atropin, strychnin) hypodermically; and by applying blisters or other counter-irritant agents to the back of the neck.

## METHYL ALCOHOL (WOOD ALCOHOL) POISONING

Methyl alcohol is extensively employed in the arts and is of interest to the physician because of the many cases of poisoning that have resulted from its use as an adulterant of whiskey and other alcoholic beverages and of cologne-water, bay-rum, etc. Its actions resemble those of ethyl alcohol, but it is excreted more slowly and is imperfectly oxidized, formic acid being the chief product of its incomplete combustion. The formic acid is rapidly eliminated by the kidneys, but gives rise to acidosis. Methyl alcohol has often proved toxic when used externally, and even the vapor of it is dangerous when ventilation is insufficient. Poisoning is much more likely to result in death than that from ethyl alcohol.

**Symptoms.**—The symptoms resemble those of ordinary alcoholic intoxication, the chief differences being the protracted coma which sometimes lasts two or three days and the more serious after-effects, particularly partial or complete blindness from destructive inflammation of the optic nerve or retina, which occurs in about one-half of all cases. The primary symptoms consist of abdominal pain, nausea and vomiting, headache, vertigo, and disturbance of vision. Later, restlessness, delirium, coma and collapse occur. The pupils are dilated and insensitive. Dyspnea is often marked. Death from respiratory paralysis may occur in from a few hours to two or three days. Occasionally the symptoms are deferred for several days and then prove rapidly fatal.

Wood and Buller,[1] found 153 cases of blindness and 122 deaths recorded up to 1904, and since then a great many additional cases have been reported. In December, 1911, 89 deaths and 5 cases of total blindness due to the use of a cheap drink containing wood alcohol occurred in a Berlin lodging house (Stadelmann[2]).

**Treatment.**—This consists of rapid evacuation of the stomach, purging, administration of respiratory and circulatory stimulants, proctoclysis with a solution of sodium bicarbonate, and, if necessary, intravenous injection of normal saline solution.

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## CHRONIC OPIUMISM

**(Opium Habit; Morphin Habit; Morphinism)**

Chronic opiumism is an uncontrollable craving for opium or one of its alkaloidal derivatives, leading to constantly increasing doses of the drug and eventually resulting in mental, moral and physical degeneration. It is usually acquired by using opium, morphin or heroin for the relief of pain or insomnia or by associating with addicts. Unfortunately, the physician himself is responsible for many cases. Neurotic individuals are especially susceptible, but normal persons not rarely become habituated to the use of opiates by taking them over a considerable period of time. According to Petty,[3] the average person acquires an addiction to morphin when the drug is used daily for a month. Morphin may be used for a longer time without causing the habit when taken by the mouth than when taken hypodermically, the difference in this respect depending upon the rate of absorption and hence upon the strength of the narcotic impression. Codein is much less likely to produce a habit than either morphin or heroin. Habitués are able to withstand enormous doses of an opiate without suffering from acute poisoning, this tolerance being due partly to an increase in the power of the organism to destroy the drug and partly to an increase in the power of resistance. The average daily oral dose of morphin for an addict is probably between 5 and 15 grains, but the daily consumption may be as high as 90 grains (McIver and Price[4]). A large proportion of addicts begin the use of drugs while still minors. Opium itself may be taken by the mouth or inhaled as smoke; morphin may be introduced by the mouth or by hypodermic injection; heroin is usually sniffed up the nostrils.

**Symptoms.**—If he is careful as to dosage, the addict may get along fairly well for years, without even his family or his associates being aware of his habit. In 3 of the cases studied by McIver and Price the duration of the addiction was over 30 years. Sooner or later, however, a more or less characteristic condition is produced, the important features being a cachectic appearance, with a pale, dry skin, disturbed digestion, obstinate constipation or constipation alternating with diarrhea, loss of flesh and strength, restlessness, irritability of temper, moodiness, with transitory periods of depression and exaltation, impairment of intellect, loss of will power and of ethical sense, and moral perversion, this last being much more pronounced, as a rule, than in alcoholism. In advanced cases the body is emaciated, the skin is sallow or pale and wax-like, the pupils are moderately dilated, the lips, tongue and

[1] Jour. Amer. Med. Assoc., Oct. 1, 1904.
[2] Berlin klin. Woch., 1912, xlix, No. 5.
[3] Petty, G. E.: The Narcotic Drug Diseases and Allied Ailments, Phila., 1913.
[4] Jour. Amer. Med. Assoc., Feb. 12, 1916.

hands are tremulous, the gait is unsteady, and the whole appearance of the patient is that of premature senility. Neuralgias and paresthesias are almost always present and impotence is common. If the drug is taken hypodermically the site of each needle puncture is shown by a minute bluish-white cicatrix. The systemic effects of heroinism are usually less severe than those of morphinism.

*Withdrawal or Abstinence Symptoms.*—When the habitué does not get his usual dose he invariably develops a group of distressing symptoms, the most constant of which are restlessness, depression, an intense craving for the drug, yawning, sneezing and lacrimation, and later vomiting, diarrhea, pains in the abdomen and limbs, profuse perspiration, exhaustion and not rarely collapse. These symptoms, which probably depend upon the formation of some unidentified toxic substance, vary in severity with the size of the dose that the patient has been taking and the rapidity with which the drug is withdrawn.

**Prognosis.**—Withdrawal of the narcotic is not excessively difficult and lasting recovery is by no means impossible, but the large majority of patients, even after they have been off of the drug for months, relapse.

**Treatment.**—Isolation in a special hospital or sanatorium is almost imperative, and the detention should be for at least a year. To avoid deception, the patient must be under the close observation of a reliable attendant throughout the entire course of treatment. As a rule, the opiate should be withdrawn rapidly (in from ten days to two weeks), but in severe cases not too abruptly for fear of collapse. The diet should consist of nutritious and easily digestible food, milk and eggs being most suitable at first. Free and persistent purgation is requisite. Hot baths and the administration of bromids may be employed to control nervousness; salicylates and acetphenetidin, to relieve pains; and scopolamin, trional and codein to produce sleep. Vomiting is best relieved by gastric lavage and the administration of bismuth subcarbonate. For circulatory weakness digitalis and strychnin are the most useful remedies. Massage, graduated exercise, a liberal diet and tonics are indicated in the convalescent stage.

Several special methods of treatment have found more or less favor, but no one method is applicable to all cases. The Lambert-Towns method consists in a rapid withdrawal of the narcotic and the administration of powerful cathartics (compound cathartic pills, blue mass, and salines) at frequent intervals, in conjunction with a mixture of belladonna, xanthoxylum, and hyoscyamus, which is given every hour, day and night, until signs of belladonna poisoning develop. In the Sceleth method the patient is given a mixture of dionin, scopolamin, pilocarpin and cascara sagrada, the doses varying with the amount of morphin the patient has been taking. On the tenth day this combination is stopped and strychnin nitrate is substituted. In the Petty method large doses of strychnin are given hypodermically in conjunction with scopolamin.[1]

## COCAINISM

Persons become addicted to cocain usually through curiosity, through association with habitués, through the use of the drug to overcome the after-effects of indulgence in morphin, or through the use of cocain in nose or

[1] These various methods of treatment are fully described in the Jour. Amer. Med. Assoc., Mar. 20, 1915.

throat sprays. A large proportion of addicts have a strong neurotic inheritance or show various stigmata of degeneration. The drug is usually snuffed, but it may be taken hypodermically. Pronounced tolerance is readily produced, and the amount of the drug consumed not rarely reaches 30 grains (2.0 gm.) or more.

The effects of cocainism are similar to those produced by the opium habit and the symptoms resulting from the withdrawal of the drug also resemble the abstinence phenomena occurring in morphinism. Cocain is more readily withdrawn than morphin and the prognosis of addiction to it is somewhat more favorable than that of opiumism.

The **treatment** of cocainism is similar to that of the morphin habit, the chief points being isolation in a special institution, rapid withdrawal of the drug, the use of nourishing food, free and persistent purgation, and the administration of sedatives, especially scopolamin, to lessen the severity of the abstinence symptoms.

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## TOBACCO POISONING

The chief toxic constituent of tobacco is nicotin. Centrally, this alkaloid first stimulates and then depresses the entire cerebrospinal axis, and peripherally, it depresses both the sympathetic and parasympathetic autonomic ganglia. Smoke from a short-stemmed pipe and from a thick cigar contains the most nicotin and cigarette smoke the least. The practice of inhaling cigarette smoke, however, compensates to some extent for its relative weakness in nicotin. The real objections to the cigarette, as summarized by Bastedo,[1] are that it makes smoking easy for the young, that it has a strong tendency to induce the habit of inhalation, and that, being small, it can be smoked at odd moments, so that the excessive cigarette smoker tends to keep himself under some influence of the drug all day long. The pleasant effects of smoking are largely psychic and not at all proportionate to the percentage of nicotin present in the tobacco, although it is probable that the alkaloid is not wholly without influence.

Smoking by one who is used to it seems to have some tendency to raise temporarily the blood pressure a few millimeters, but the effects are by no means constant, even in the same individual. The evidence is incontrovertible that nicotin is capable of inducing various cardiac irregularities, similar to those resulting from stimulation of the cardiac nerves, either singly or together or from stimulation of one and depression of the other. These disturbances appear to be merely functional and soon subside upon the discontinuance of the tobacco. The evidence that excessive smoking of itself can produce organic changes in the heart or bloodvessels is not so convincing although certain investigations point in this direction. Smokers, especially cigarette smokers, have frequently been found to show less mental efficiency than others free from the tobacco habit, but whether this deficiency is dependent upon the smoking itself or is a result of a weak intellectual capacity that led to an excessive use of tobacco is not clear.

**Symptoms of Chronic Tobacco Poisoning.**—Susceptibility to nicotin varies considerably in different persons. It is greater in the young than in the old, and is increased by sedentary habits, indoor-living, and an inherited neuropathic tendency. Chronic tobacco poisoning may show itself in

[1] Bastedo: Materia Medica Pharmacology and Therapeutics, second edit., p. 433.

local irritant effects or in disturbances of the digestive tract, circulatory system, nervous system or special senses. A tickling cough, expectoration of mucous or mucopurulent secretion, and hoarseness frequently occur as evidences of irritation of the mucous membrane of the throat and larynx. Anorexia, heartburn, and irregular action of the bowels are not uncommon. Occasionally, chronic tobacco poisoning appears to be wholly responsible for the hyperchlorhydric syndrome. The most serious disturbances are those affecting the heart. In young smokers palpitation, breathlessness upon exertion and irregularity of the heart are the chief manifestations. Occasionally, syncope ensues. In middle-aged smokers there may be attacks of precordial pain of an anginoid character. Even when true angina pectoris exists as a result of causes other than nicotin poisoning, marked improvement often follows the removal of the tobacco. Extra-systoles seem to depend in some cases upon excessive smoking, and even heart-block and auricular fibrillation have been ascribed to the excessive use of tobacco.

Dizziness, headache, mental sluggishness, insomnia, lack of energy, irritability, depression and tremors are sometimes caused by the continued absorption of nicotin. More rarely amblyopia develops as a result of retrobulbar neuritis. Ophthalmoscopic changes may be absent or there may pallor of the optic disc. The *prognosis* of tobacco poisoning is good. In nearly all cases the symptoms disappear upon withdrawal of the tobacco. In severe cases no marked improvement may occur until the abstinence has been continued for several weeks. In the treatment of myocardial insufficiency or arterial hypertension from any cause it is usually advisable to withhold tobacco or to reduce its use to a minimum.

## CHRONIC LEAD-POISONING

(Plumbism; Saturnism)

**Etiology.**—Chronic lead-poisoning is caused by the slow absorption of lead and the accumulation of the metal in the system. As long as excretion keeps pace with absorption symptoms do not develop. The poison may enter the body through the respiratory tract, through the gastro-intestinal tract, or through the skin. Lead dust in the air is especially dangerous, although doubtless a part of the dust that is breathed into the nose and mouth is swallowed. Cutaneous absorption of non-water-soluble compounds of lead is relatively unimportant (Weyl, Legge, Oliver, Edsall). All forms of lead are not equally poisonous. Of the compounds used in industry, the suboxid, which forms on the surface of melted lead, red lead and the carbonate are probably the most dangercus.

Plumbism may result from the accidental introduction of lead into the system through drinking water, through canned goods (solder), through candies or cakes colored with lead pigments,[1] or through hair dyes containing lead; it may be brought about by the too prolonged use of the salts of lead for medicinal purposes or through taking diachylon (lead plaster) as an abortifacient,[2] but much more frequently it is induced in workmen who are exposed to the dust or fumes of lead or who handle the metal or paints containing it. Indeed, of all so-called industrial poisons lead is the most productive of ill health. An occupation involving the use of lead is danger-

[1] Stewart, Medical News, Dec. 31, 1887, reported 64 cases in children from eating buns colored with chrome yellow.

[2] See article by Hall and Ransom, Brit. Med. Jour., Feb. 24, 1906.

ous in proportion to its dustiness. Among 140 or more trades that entail exposure to lead the best known are lead mining and smelting, working in white lead and lead colors, making type, pipe and other articles of lead, plumbing, printing, stereotyping, lithography, tinning, coach polishing (sandpapering dried paint), production of storage batteries and accumulators, and glazing pottery, bath-tubs, tiles, etc. Among the less conspicuous lead-using industries may be mentioned zinc smelting, brass and nickel polishing, file making (old method) finishing cut-glass, working with tin-foil and aluminum-foil, diamond cutting, commercial illustration, manufacture of rubber goods, laying electric cables, and handling of lead-dyed artifical flowers, yarns and wall-paper.

Individual susceptibility varies considerably. The incidence of plumbism is proportionately greater among female workers than among male workers. Age is not without influence, the young being more readily affected than the old. Alcoholism, reduced vitality from any cause, and unhygienic habits increase the liability to poisoning. The quantity of lead required to produce poisoning is not definitely known. The lowest estimate is that of Brouardel, who places it at 1 mg. per day. The length of exposure necessary to the development of symptoms varies according to circumstances from a few days to many years.

**Symptoms.**—The early symptoms are, as a rule, indefinite, but are significant when occurring in a person who has been exposed to lead. There may be pallor, general weakness, loss of flesh, trembling of the fingers, pains in the muscles and joints (usually described as rheumatic), anorexia, digestive disturbances, and constipation, or constipation alternating with diarrhea. The later and more characteristic manifestations are intestinal colic, a blue line on the gums, muscular paralysis, and basophilic degeneration of the red blood-corpuscles.

*Colic.*—This is usually preceded by digestive derangements and accompanied by obstinate constipation. The pain, which is probably an effect of vagus stimulation, occurs in paroxysms lasting from a few seconds to an hour or more and is commonly most intense about the umbilicus, although it may be diffuse. In severe attacks the abdominal wall is rigid and retracted, the blood-pressure is high, and not rarely the pulse is small and infrequent. Vomiting occurs in about one-half of the cases. The paroxysms often continue to appear over a period of several days. Relapses are common and occasionally occur even without any renewal of exposure. Care must be taken not to confuse lead colic with other abdominal pains, such as occur in appendicitis, peptic ulcer, cholelithiasis, renal calculus, and sometimes in tabes dorsalis, floating kidney, and aneurysm of the abdominal aorta.

*Blue Line.*—This consists in bluish or grayish-black line at the margins of the gums, especially about the incisor and canine teeth. It is due to the precipitation of lead sulphide, which compound is formed from the circulating lead through the action of hydrogen sulphide that is given off by decomposing particles of food. It is fairly constant, and while it does necessarily imply lead poisoning, it signifies adsorption of the metal. If the teeth are well cared for and the gums are healthy the lead-line may be absent. Blackish deposits on the teeth themselves may be excluded by pushing a small piece of white paper between the edge of the gum and the teeth (Stewart). Similar lines are produced by silver, bismuth, copper and other metals.

*Paralysis.*—This is apparently due to degeneration of the peripheral nerves, especially of their terminal filaments, although changes have occasionally been observed in the nerve-cells of the anterior horns of the spinal cord (Déjérine-Klumpke, Spiller, Nissl, Stieglitz). The paralysis is almost

always bilateral and in the large majority of cases is confined to the muscles which are supplied by the musculospiral nerve below the branch which goes to the supinator longus. It usually shows itself, therefore, in weakness of the extensors and in the characteristic "wrist-drop." In severe cases the intrinsic muscles of the hands also become involved. Eventually the affected muscles undergo atrophy and yield the reactions of degeneration. A tremor is often observed in the hands and fingers, but pain is exceptional. Objective sensory changes are slight or wholly wanting, and pronounced contractures are uncommon. The predisposition of the extensors of the arm is probably due to the greater use of these muscles (Stieglitz,[1] Edinger,[2] and Teleky[3]). Much less frequently the muscles of the upper arms are affected, and occasionally the muscles of the legs (peroneal group and extensors of the toes), especially in children, become paralyzed. Still more rarely the ocular muscles, the laryngeal muscles, or the intercostal muscles are involved or the paralysis begins in the feet and spreads upward, as in Landry's disease. Ordinary polyneuritis is very uncommon, but general sensory disturbances, especially paresthesias, are somewhat frequently observed. Painful cramps of the muscles, especially those of the calves, may also appear. Relapses often occur when patients return to their work and occasionally even without any renewal of exposure.

*Basic Granulation of the Erythrocytes.*—This sign is a valuable aid in the diagnosis of plumbism, although it is sometimes absent and it may occur in other anemias. The characteristic feature is the appearance of granules of varying size in many or a few of the red cells when these are stained with basic dyes. Accompanying the basic granulation there is usually some reduction in the number of red cells and the percentage of hemoglobin, but, as a rule the pallor of the skin is out of all proportion to the actual anemia. The pallor has been ascribed to vasoconstriction.

*Cerebral symptoms* (encephalopathy) in plumbism are relatively rare, but sometimes develop very suddenly in severe cases and in alcoholics. Intense headache, epileptiform convulsions, delirium and coma are the most common. Occasionally, the symptoms resemble those of paretic dementia. Postmortem examination of the brain in encephalopathy has shown in some instances slight thickening of the pia, edema, and scattered small hemorrhages. It is important not to confuse true encephalopathy with uremia. *Chronic nephritis* (cirrhosis of the kidneys) and *arteriosclerosis* are both common in lead workers. The urine in many cases shows not only a small amount of albumin and a few casts, but also traces of hematoprophyrin. Some relation seems to exist between plumbism and *gout*, the latter being relatively frequent in lead workers.

*Amblyopia*, without ophthalmoscopic changes or with evidences of optic neuritis, occasionally develops. In addition to causing a deposition of lead sulphid in the gums, the continued absorption of lead is believed to favor the occurrence of *caries of the teeth* and *gingivitis*. *Parotitis*, probably due to ascending infection from the mouth, has been described by a number of writers. Sailer and Speese found *gastric achylia* in 10 out of 12 subjects of saturnism. Lead has an unfavorable influence upon gestation and upon offspring . From 20 to 25 per cent. of the pregnancies occurring in the wives of men giving evidences of plumbism terminate in *miscarriages* (Verhaeghe, Harris),[4] and a large proportion of the surviving children of males

[1] Arch. f. Psychiatrie, 1892, xxiv.
[2] Deutsch. med. Woch., 1904, Nos. 45, 49, 52.
[3] Zur Kasuistik. d. Bleilähmung. D. Z. f. Nervenheilk., 1909, vol. xxxvii.
[4] Amer. Jour. Med. Sci., Jan., 1919.

affected by lead die a short time after birth (Legge,[1] Mott[2]), or are deficient in vitality.

**Diagnosis.**—This rests upon the history of exposure, the blue line, colic, bilateral wrist-drop without involvement of the supinator longus, pallor, basic degeneration of the erythrocytes, and the demonstration of lead in the urine. The absence of any of these signs is, of course, without significance if other characteristic features are present and particularly if these are associated with a clear source of poisoning. The occurrence of increasing weakness, pallor and digestive disturbances without obvious cause in a laborer should always lead to a careful inquiry into the nature of his occupation.

**Prognosis.**—In the absence of any pronounced organic changes in the bloodvessels or kidneys and of encephalopathy the outlook is favorable. Lead palsy usually disappears in from a few months to a year, but when it is of long duration and accompanied by marked atrophy the prognosis for complete recovery is not good. Cerebral symptoms are always of grave significance.

**Prophylaxis.**—Much can be done to prevent plumbism in lead-work establishments. The requisites are a thorough knowledge on the part of both employer and employee of the danger that working in lead entails, periodic medical inspection of workers, the collection of dust and fumes, as far as possible, at the source by proper exhaust systems, the substitution of vacuum cleaning for dry sweeping, thorough ventilation, the use of respirators by men engaged in dry processes, provision of ample bathing facilities, general personal cleanliness, change of outer clothing before leaving the works, the avoidance of food in any place where work is carried on, the free use of protein food before beginning work, prohibition of smoking and chewing during work, and complete exclusion of alcohol.

**Treatment.**—The indications are to prevent further absorption of the poison, to favor elimination, and to relieve the immediate symptoms. Removal from exposure to lead is imperative. Potassium iodid, in doses of 5 to 10 grains (0.3—0.6 gm.) thrice daily, is believed to hasten elimination of the lead, although the manner of its action is not apparent. Sulphur baths are also recommended. These are prepared by mixing in a wooden tub 3 or 4 ounces (90.0—120.0 gm.) of potassium sulphuret with about 20 gallons (75.0 liters) of water. Constipation should be relieved by saline cathartics, preferably Epsom salt, or by oil enemas. Belladonna in full doses is a useful adjuvant, as the constipation is of the spastic type. Colic will require hot applications and hypodermic injections of morphin and atropin. Benzyl benzoate (5 to 20 minims—0.3–1.3 mils), every two hours, is helpful, but less effective as an antispasmodic than atropin. For the paralysis massage, electricity and strychnin should be used.

## MERCURIAL POISONING

**Acute Poisoning.**—The most acute form of mercurial poisoning is that resulting from swallowing tablets or a solution of corrosive sublimate. The symptoms usually appear within half an hour and consist of a metallic and astringent taste, severe abdominal pain, vomiting and purging of mucous and bloody material, and signs of collapse. Corrosion of the mouth or throat may also occur. Unless death ensues within a few hours, which is excep-

[1] Jour. Hygiene, 1901, i, 96.
[2] Brit. Med. Jour., Oct. 28, 1905.

tional, symptoms of acute stomatitis (salivation, congestion and swelling of the gums, etc.), of acute colitis (bloody diarrhea with tenesmus) and of acute nephritis (oliguria or anuria, albuminuria, etc.) usually supervene. Occasionally neither the nephritic nor the dysenteric features show themselves for several days or until there has been complete recovery from the corrosive effects of the drug. Death usually occurs within a week, but sometimes slow recovery ensues even after anuria has lasted for several days.

Postmortem examination shows corrosion and inflammation of the alimentary canal, sometimes with membranous colitis; acute nephritis, often with calcareous "infarcts" in the uriniferous tubules; and degenerative changes in the other solid organs.

**Treatment.**—Egg-white should be given at once to precipitate any mercuric chlorid that has not yet entered the duodenum, and then the stomach should be emptied, preferably by the stomach-tube. To remove the poison from the bowel the gastric lavage should be followed by the administration of Epsom salt (1 ounce—30.0 gm.), and by irrigation of the colon. It is advisable to repeat the enteroclysis twice daily as the mercury is excreted chiefly by the colon. Hot packs and alkaline diuretics are of service in promoting elimination through the skin and kidneys respectively. Lambert and Patterson[1] recommend hourly liquid by the mouth, 8 ounces (240.0 mils) of milk, alternating with 8 ounces (240.0 mils) of the following mixture:

| | |
|---|---|
| Potassium bitartrate | |
| Sugar, of each | ℥i (4.0 gm.) |
| Lactose | ℥iv (15.0 gm.) |
| Lemon juice | f℥i (30.0 mils) |
| Boiled water, to make | Oj (480.0 mils) |

In anuria repeated flushing of the colon with hot water, 110° F. (44° C.), and intravenous injections of saline solution should be tried. In a few instances decapsulation of the kidneys has been successful.

**Subacute Poisoning.**—This is observed most frequently as a result of the use of mercury for medicinal purposes, the doses being too large or the treatment too long continued, but it is also seen in sequence to acute poisoning. The most conspicuous feature is stomatitis, which is probably due partly to the direct irritant action of mercury that is excreted in the mouth, partly to the precipitation of mercuric sulphid in the capillary endothelium, (Almkvist[2]) and partly to secondary infection. The susceptibility to mercurial stomatitis varies greatly. It is increased by poor hygienic conditions of the mouth and teeth and by chronic nephritis. Even a grain of calomel has been known to produce it. The earliest symptoms are a metallic taste, salivation, fetor of the breath, and redness and soreness of the gums. If the administration of the drug is continued glossitis develops with marked swelling of the tongue, the gums become spongy and ulcerated, the salivary glands enlarge, the teeth loosen and fall out, and finally necrosis of the maxillary bones ensues. At the same time the general health is more or less affected. The patient becomes pale and loses flesh. Fever, chilliness, thirst and anorexia not rarely occur, and after a time symptoms of colitis and of nephritis may supervene.

**Treatment.**—The administration of mercury should be suspended as soon as the slightest tenderness of the gums appears. The mouth should be rinsed at frequent intervals with a saturated solution of potassium chlorate

[1] Arch. Int. Med., 1915, 16, 865.
[2] Dermat. Zeitsch., 1912, 19, 949.

or alternately with this and a soluton of hydrogen dioxid (1 to 3 of water). In severe cases the affected parts may be painted with a solution of argyrol (20 per cent.) or a solution of silver nitrate (5 to 10 per cent.). To check the excessive flow of saliva, atropin sulphate, $\frac{1}{125}$ of a grain (0.0005 gm.), may be given once or twice a day. Morphin is sometimes required at night to relieve pain and produce sleep. Later, tonics may be of service in combating anemia and exhaustion.

**Chronic Poisoning.**—This is observed chiefly in workmen who handle mercury or who are exposed to its fumes. Thus, it occurs in makers of mirrors, thermometers, barometers, incandescent electric bulbs, felt hats, and explosives derived from fulminate of mercury. Occasionally it is induced by the prolonged use of mercury as a medicine. Its chief manifestations are stomatitis with salivation, gastrointestinal disturbances, muscular weakness, emaciation, cachexia, and various nervous and psychic disorders, especially tremors and mental impairment, with irritability and depression. Multiple neuritis has also been described, but according to Starr,[1] no case can be found which is not open to objection.

**Treatment.**—Removal of the patient from exposure to the mercury is imperative. Tonics are usually indicated. Free water drinking, active catharsis and warm baths are useful in promoting elimination. The administration of potassium iodid is also recommended, but it is of doubtful value.

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## ARSENIC POISONING

**Acute Poisoning.**—This is usually suicidal or accidental and is due, as a rule, to white arsenic (arsenic trioxid) or to Paris-green (aceto-arsenite of copper). It is characterized by severe abdominal pains, persistent vomiting, profuse diarrhea with "rice-water" stools, great thirst, oliguria, muscular cramps, cyanosis, and collapse. Death, which usually occurs in from twenty-four hours to three days, is often preceded by delirium, convulsions, and coma. If recovery ensues, the symptoms of acute poisoning may be slowly replaced by those of chronic poisoning. Occasionally cases are encountered which depart somewhat from the usual type; thus there may be a rapid termination in collapse or coma without any pronounced abdominal symptoms; sometimes a temporary remission in the symptoms occurs about the third day, and this is followed, as in the case of phosphorus poisoning by jaundice, delirium and coma; again, there may be in addition to the gastrointestinal symptoms, an extensive urticarial or vesiculo-papular rash. It is difficult to fix upon the minimum fatal dose of arsenic trioxid, since much that is ingested may escape absorption. According to Taylor, about 2 grains (0.13 gm.) is the minimum fatal dose for an adult, but cases are on record in which much larger amounts have been swallowed without destroying life. After death the chief macroscopic changes are found in the alimentary canal. A large quantity of serous fluid is usually present, the intestine itself is edematous, and the epithelial covering is more or less exfoliated. There is, however, no pronounced corrosion of the tissues. Microscopic examination reveals fatty changes in the intestinal epithelium and in the liver, kidneys, heart and muscles.

*Treatment of Acute Poisoning.*—The poison should be removed from the alimentary canal by thorough lavage and the administration of a saline

[1] M. Allen Starr; Organic and Functional Nervous Diseases, Phila., Second edition, 1907, p. 139.

cathartic. The best chemical antidote is freshly prepared ferric hydroxid with magnesia, administered while still moist in doses of a tablespoonful every fifteen minutes. This compound is harmless and acts by forming a less poisonous iron arsenate. Demulcents and bismuth subcarbonate may be employed to allay gastro-intestinal irritation, morphin and atropin to relieve pain and cramps, and saline infusion to combat anhydremia and collapse.

**Chronic poisoning** may be a sequel of acute poisoning, may follow the prolonged use of the drug for medicinal purposes, may result from the use of foods or liquors contaminated with arsenic, may be produced by the constant inhalation of dust arising from wall-papers, furs, artificial flowers or other fabrics containing arsenic, or may be acquired by workers who handle arsenic or who are exposed to arsenical fumes. It may be manifested by gastro-enteritis, catarrh of the upper air-passages, anemia, peripheral neuritis, and various rashes of an erythematous or inflammatory type. Pigmentation of the skin has also been observed. Polyneuritis is occasionally seen in children to whom the drug is being given for chorea. Railton has reported four cases in which the paralytic phenomena did not appear until from 1 to 3 weeks after the drug had been discontinued. In 1900 more than 3,000 cases of poisoning occurred in England from drinking beer containing $\frac{1}{77}$ to $\frac{2}{77}$ of a grain (0.01–0.02 gm.) per gallon. The arsenic was traced to the sulphuric acid which was made from arsenical pyrites and which was used in producing the glucose employed in the brewing.[1] In this epidemic gastro-intestinal symptoms were not marked, the chief manifestations being numbness and tingling in the hands and feet; a sense of burning in the feet and painful flushing, resembling erythromelalgia; and certain cutaneous lesions, consisting of melanosis, herpes zoster, hyperidrosis, hyperkeratosis of the palms and soles, and pemphigoid eruptions.

In addition to causing hyperkeratosis of the hands and feet prolonged arsenical medication may result in other lesions of the skin indicative of increased cellular proliferation. Thus, it may lead to horny growths, multiple warts and, perhaps, epithelioma. In 1899 Hartzell[2] collected 11 cases of epithelioma occurring in psoriasis and apparently due to the prolonged use of arsenic.

**Treatment of Chronic Poisoning.**—The indications are to prevent the further absorption of arsenic, to favor elimination, and to improve the general nutrition. Potassium iodid has been recommended but it is of doubtful value. The treatment of arsenical neuritis does not differ from that employed in other forms of toxic neuritis.

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## CARBON MONOXID POISONING

### (Illuminating-gas Poisoning)

Carbon monoxid, which is the principal product of the incomplete combustion of carbonaceous matter, is responsible for more deaths than the total of all other gases. To it are chiefly due the poisonous effects resulting from the inhalation of illuminating gas, of the fumes from coal stoves and charcoal fires, of the "after-damp" from explosions in mines, of the smoke in burning buildings, etc. Illuminating gas formed by the dry distillation of coal (so-called coal gas) contains from 6 to 8 per cent. of carbon-monoxid and is much less dangerous than that formed by mixing petroleum vapor with

[1] Lancet, 1900, vol. i, p. 1610.
[2] Amer. Jour. Med. Sci., Sept., 1899.

the gas produced by blowing live steam over hot coal (so-called water gas), and which contains about 30 per cent. of carbon monoxid. The peculiar odor of illuminating gas is due solely to sulphur compounds which are harmless. Carbon monoxid is unirritating and inert, but it unites readily with hemoglobin and thus decreases the normal oxygen-carrying capacity of the blood. In this way oxygen deficiency (anoxemia) ensues and gives rise to asphyxia. Carbon-monoxid hemoglobin is not a very stable compound and if respiration is maintained and sufficient oxygen is present the carbon monoxid is set free and the hemoglobin restored in two or three hours. The persistence of coma in the presence of an excess of oxygen and the occurrence of grave nervous symptoms after the phenomena of acute poisoning have disappeared are not due to retention of gas, but are the results of injury to the brain and other organs by the insufficiency of oxygen supplied to them while the patient was breathing the gas (Henderson[1]). As a rule, a person dies who has breathed air containing 0.4 per cent. of carbon monoxid for an hour or air containing 0.2 per cent. for four or five hours. With from 2 to 5 per cent. of the gas in the air death occurs within a few minutes. Frequent exposure to low concentrations of carbon monoxid (0.01–0.02 per cent.) sometimes causes unpleasant symptoms, but rarely has a cumulative harmful effect, for the oxygen deficiency in the blood eventually results in polycythemia and the establishment of a certain degree of tolerance to the gas.

The most constant changes in the body after death from acute poisoning are general hyperemia, scattered small hemorrhages in the various organs, and parenchymatous degeneration of the heart, liver, kidneys and muscles. Pulmonary edema and bronchopneumonia are also common findings. Spiller and others have found in cases in which there has been only partial recovery, softening of the lenticular nuclei, a result of degenerative changes in the supplying arteries.

**Symptoms.**—Acute poisoning is characterized by severe headache, throbbing of the vessels, vertigo, muscular weakness, nausea and vomiting, and then stupor, coma, relaxation of the sphincters, muscular twitchings and sometimes epileptiform convulsions. The respiration is labored and stertorous; the pulse at first may be slow from stimulation of the vagus center or impairment of auriculoventricular conduction by the anoxemia (Haggard[2]), although later it is usually rapid; the skin often presents a pinkish hue, which is due to the cherry-red color of the circulating CO-hemoglobin, and just before death hyperpyrexia may ensue. Death is usually due to respiratory failure. Occasionally it is caused by the aspiration of vomitus. Even after the restoration of consciousness there is a pronounced tendency to pulmonary edema and pneumonia. Coma may last from a few minutes to forty-eight hours or even several days. Recovery may occur in apparently desperate cases, although coma that persists for more than 36 hours usually proves fatal. Not infrequently recovery is only apparent and after the lapse of several hours, days, or weeks grave *sequelæ* may develop. Thus, partial or complete loss of vision, paralysis of central or peripheral origin, amnesia, persistent headache, mental confusion, dementia, choreiform movements, polyneuritis, or permanent cardiac weakness may occur.

**Chronic poisoning** resulting from continued exposure to low concentrations of the gas may be manifested by headache, dizziness, languor, intellectual weakness, digestive disturbances, and general asthenia.

**Treatment of Acute Poisoning.**—This consists chiefly in the prompt removal of the patient from the gas-laden atmosphere, the practice of artificial

[1] Jour. Amer. Med. Assoc., Aug. 19, 1921.
[2] Amer. Jour. Physiol., July, 1921.

respiration, and the forced inhalation of oxygen or preferably of oxygen and carbon dioxid, for the loss of the latter as a result of the excessive breathing tends to depress still further the respiration. Bleeding, followed by direct transfusion of blood or saline infusion, seems to be helpful (Wormmueller, Crile and Lenhart), although Henderson believes that these measures are not only superfluous, but are likely to be harmful. Subcutaneous or rectal injections of warm saline solution may be useful in supplying water to the tissues. Intravenous injections of a 3 per cent. solution of sodium bicarbonate have been employed to combat acidosis, which is often present, but no pronounced benefit has been observed from this measure. External heat is required if the body temperature is below normal. Stimulants, such as, caffein, strychnin, and digitalis, are necessary if the circulation is weak.

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## FOOD POISONING

1. Poisoning may result from using as food certain animal or vegetable tissues, which are in and of themselves injurious. Such substances have been designated *pseudo-foods*. Thus, certain fish are always poisonous and others become so during the spawning season. Intoxication by certain mushrooms, or fungi, is of common occurrence. A chronic nervous disease, with paralytic features, arises from the habitual use as food of the peas of certain species of *Lathyrus* (vetchlings). Cases of illness from the use of soup prepared from sour-grass, a species of sorrel very rich in oxalic acid, have recently been reported (Rosenau).[1]

Green and growing parts of potatoes, which are relatively rich in the glucosid, solanin, may cause a severe intoxication, characterized by abdominal pains, vomiting and diarrhea.

2. Food may be made poisonous by the presence of *chemical substances* which have been introduced accidentally or in order to improve its appearance or keeping qualities. Illness from this cause, however, is comparatively uncommon. A notable example was the English "beer epidemic" of 1900, in which more than 3000 cases of poisoning were traced to the accidental presence of arsenic in a certain brand of beer. Poisoning from the use of canned food is almost always of bacterial origin, although in rare instances it may be due to lead, tin, or other metals derived from the vessel containing the food.

3. Formerly many cases of food-poisoning were attributed to *ptomains*, or intermediate cleavage products of protein decomposition, but it is now known that these bodies are very rare causes of illness. Some of them, like cholin and neurin, are toxic when introduced into the body parenterally, but so far none of them have been shown to be especially harmful when taken by the mouth.

4. The large majority of cases of food poisoning are due to the action of living *bacteria or their toxins*. The most important food-borne infections are typhoid fever, paratyphoid fever, cholera, tuberculosis, and epidemic streptococcus sore throat. In some instances pathogenic bacteria have been present before death in the animal from which food was obtained, and in other instances food that was originally wholesome has been infected through careless handling or the agency of flies. In a comparatively large group of cases the infective agent is the *Bacillus enteritidis* of Gärtner. When this organism, which belongs to the colon-typhoid group, is taken into the body

[1] Med. Clin. of North America, Mar., 1919.

with food or drink it produces symptoms closely resembling those of paratyphoid infection or of an abortive attack of typhoid fever. Other outbreaks of food-infection have been attributed to *Bacillus proteus*. The best established food-borne intoxication resulting from the ingestion of pre-formed bacterial toxins is that known as *botulism*. The toxin is produced in canned fruits and vegetables, potted meats, sausages, etc. by the *Bacillus botulinus*.

5. **Anaphylactic reactions** to certain foods are frequently observed. The peculiar supersensitiveness is caused by the entrance into the blood of intact foreign protein molecules. The latter serve as antigens and induce the formation of specific antibodies (allergins), which, alone or in conjunction with non-specific complement, split the foreign protein, setting free poisonous products, or anaphylatoxins. Ordinarily the protein molecule is rendered harmless by digestion, but under certain conditions which are not clearly understood it may pass from the intestine into the blood unchanged, and there through a process of cleavage liberate anaphylactic poison. Many food proteins, both animal and vegetable, have been demonstrated conclusively to be the cause of disease. Eggs, milk, fish, shell-fish, meat and certain fruits, especially strawberries, are the foods most likely to excite anaphylactic reactions. Not a few individuals are sensitized to more than one protein.

Asthma, due to contraction of the bronchial muscles, is one of the most common manifestations of anaphylaxis. In some cases the symptoms are those of a severe gastro-intestinal disturbance, and consist of abdominal pain, vomiting, and purging. The so-called "idiosyncrasies" observed in persons who regularly suffer from gastro-intestinal derangements, urticaria, etc., after eating certain foods seem to depend upon an acquired or inherited supersensitiveness to the particular proteins involved. Certain cases of angioneurotic edema are probably of an anaphylactic nature. Occasionally the sensitization is so marked, that swelling of the tongue, edema of the larynx and intense cyanosis appear as soon as the offending protein is introduced into the mouth. Other effects of anaphylactic intoxication are a fall of temperature, leucopenia, eosinophilia, and diminished coagulability of the blood. According to Longcope,[1] repeated anaphylactic reactions may result in degenerative changes in the kidneys, liver, heart and other organs. The particular form of food protein to which the patient is sensitized may be determined by means of the cutaneous reaction. When a minute quantity of a solution of the offending protein is injected into the superficial epithelial layers or is rubbed into a slight abrasion it quickly produces a definite wheal with a surrounding zone of hyperemia.

## BOTULISM

Botulism[2] is a form of poisoning caused by a toxin which is produced in foods outside of the body by the *Bacillus botulinus*, a spore-bearing anaerobe. This organism, which is widely distributed in nature, finds favorable conditions for its proliferation not only in sausages and potted meats, but also in canned vegetables and fruits. The majority of outbreaks on record in the United States have been due to canned vegetables or fruits. Foods prepared in the household are more likely to cause botulism than those prepared in canning establishments in which steam under pressure is used. The spores of B. botulinus, especially when young, are very resistant to heat. According to Weiss[3] they are destroyed within 40 minutes at 221° F. (105° C.) and within 6 minutes at 248° F. (120° C.). The toxin, which alone is responsible

[1] Jour. Exp. Med., 1913, 678; 1915, 793.
[2] Lat., *botulus*, sausage.
[3] Jour. Infect. Dis., 1921, xxviii, 70.

for the illness, is produced only outside of the body and is rapidly destroyed by heat. Signs of spoilage from B. botulinus are gas bubbles in the jar, an odor resembling that of rancid cheese, and a mushy appearance of the solid parts (Burke[1]). Even tasting such food may prove fatal. There is no danger of botulism from uncooked vegetables or fruits or from those freshly cooked.

The **symptoms** of botulism develop as a rule in from 12 to 72 hours after the contaminated food has been eaten and are chiefly referable to the nervous system, being due apparently to thrombotic occlusion of small blood vessels and secondary retrogressive and inflammatory changes in the brain-stem (Wilbur and Ophüls,[2] Semerak[3]). Vertigo, ocular palsies—ptosis, mydriasis diplopia, and amblyopia—difficulty in deglutition and phonation, and extreme muscular weakness are the important manifestations. Nausea and vomiting may or may not occur at the beginning of the attack. Fever is absent. Up to 1920 there were 40 recognized outbreaks of botulism in the United States with 150 cases and 64.6 per cent. mortality (Wells and Blankinship[4]). Death, which usually occurs in from 1 to 3 days, is caused by respiratory or circulatory failure or by aspiration pneumonia, as in bulbar palsy. Recovery may occur within a few days or only after weeks of illness.

**Prophylaxis.**—This comprises the use of only sound fruit and vegetables for canning, clean methods of handling, prolonged cooking, and the rejection of canned food that is in the least suspicious. Boiling for five minutes completely destroys the toxin.

**Treatment.**—The stomach should be emptied by lavage and an active purgative should be given, even if a long time has elapsed since the poisonous food was eaten. Circulatory and respiratory stimulants are indicated. Feeding by the stomach-tube may be necessary. Oxygen has been of service in some cases. If used early, antibotulinus serum may be helpful. Polyvalent A and B antitoxin should be used if the prevailing type of intoxication is unestablished. The type of toxin may be determined by exposing chickens to the poisonous food, these birds being highly refractory to Type B toxin, but developing paresis and coma within a few hours when given food containing Type A toxin (Graham and Schwarze[5]).

## MUSHROOM POISONING

According to Ford[6] the poisonous fungi belong mainly to three classes: (1) Those containing muscarin, which acts on the nervous system; (2) those producing degenerative changes in the viscera; and (3) those causing intense gastro-intestinal irritation. In this country the greater number of cases of mushroom poisoning are due to *Amanita phalloides* and *Amanita muscaria*.

*Amanita phalloides* (deadly agaric) has a white or slightly brownish cap with persistently white gills; its stem often arises from a cup, is bulbous at the base, and has a collar (annulus) near the cap. Its poisonous properties are due to a toxin, which produces degenerative changes in the internal organs. Prolonged boiling lessens its toxicity. The *symptoms* of poisoning set in after a latent period of from 8 to 15 days and consist of abdominal pain, vomiting, diarrhea, cyanosis, great prostration, suppression of urine, delirium

[1] Jour. Amer. Med. Assoc., Jan. 11, 1919.
[2] Arch. Int. Med., Oct., 1914.
[3] Jour. Infect. Dis., Aug., 1921.
[4] Jour. Amer. Med. Assoc., Jan. 10, 1920.
[5] Jour. Amer. Med. Assoc., June 18, 1921.
[6] Jour. of Pharmacol., 1911, 2, 285.

and collapse. Jaundice may also occur. Some of the symptoms are apparently due to renal insufficiency (Clark, Marshall and Roundtree). Death is the rule, and usually it occurs within a few days, but it may be delayed two or three weeks.

As there is no physiologic antidote, *treatment* consists in evacuating thoroughly the alimentary canal, sustaining the patient's strength and combating symptoms as they arise.

*Amanita muscaria* (fly agaric) has a yellow or orange-colored cap with numerous scales; its stem bulges at the base and is surrounded by a collar or annulus. It contains muscarin, which produces effects resembling those of pilocarpin. In poisoning the *symptoms* usually appear within an hour after the fungi have been eaten and consist of abdominal pains, vomiting, diarrhea, profuse salivation and sweating, delirium and collapse. *Treatment* consists in washing out the stomach and colon, giving atropin, which is antidotal, and warding off collapse. The poison is quite rapidly eliminated and recovery usually occurs when treatment is instituted promptly.

In poisoning by toadstools containing only irritant principles, such as *Lactarius torminosus, Entoloma sinuatum*, etc., the symptoms are merely those of severe gastro-enteritis.

## LATHYRISM

Lathyrism is a chronic nervous disease due to the habitual use as food of the peas of certain species of *Lathyrus*. At present it is observed chiefly in India. The *symptoms* consist of stiffness and trembling in the legs, followed by spastic paralysis and a tendency to crossed-leg progression. The tendon-reflexes are exaggerated, sensation is perverted, control of the sphincters is impaired, and sexual power is lost. The upper part of the body is unaffected. The disease does not seem to cause death directly, but when fully developed it is incurable.

## ERGOTISM

Ergotism is a form of poisoning caused by the use of flour contaminated with a fungus (*Claviceps purpurea*) growing in the grain of cereals, especially rye. It is very rare at the present time, but formerly it was common among the poorer classes of Europe. Acute and chronic forms occur.

**Acute ergotism** is characterized by symptoms of gastro-enteritis—abdominal pain, nausea, vomiting and diarrhea, and various nervous phenomena, such as headache, vertigo, paresthesias, epileptiform convulsions, delirium, stupor and coma. In pregnant women abortion usually occurs. Death is due to circulatory failure.

**Chronic ergotism** assumes two types: the spasmodic and the gangrenous. In both types the early symptoms usually consist of gastro-intestinal derangements, debility, headache, dizziness, disturbance of vision, and various paresthesias, particularly formication. Later, in the spasmodic type muscular twitchings develop, especially in the extremities, and pass into tonic and clonic spasms and sometimes into permanent contractures. General epileptiform seizures and psychic disturbances, mimicing various forms of insanity, may also occur. Ultimately, the symptom-complex may resemble more or less closely that of tabes dorsalis. In the gangrenous type the gastro-intestinal disturbances and paresthesias are followed by sloughing of the tissues in certain parts of the body, especially the fingers, toes, ears and nose. In both forms of chronic ergotism the symptoms are due to persistent constriction of the arterioles.

# Food Deficiency Diseases

## RICKETS

(Rachitis)

**Definition.**—Rickets is a common disease of infancy characterized by a deficiency of calcium salts in the growing bones and general disturbances of nutrition.

**Etiology.**—Rickets usually occurs toward the end of the first or during the second year, although cases in the newborn have been reported, and it is said to develop in rare instances as late as puberty. Overcrowding, lack of sunlight, insanitary conditions, and a defective diet favor its occurrence and hence the disease is especially prevalent in large cities and among the children of the poor. Probably as a result of indoor confinement and the poorer quality of the milk in winter, the disease is more prone to develop in the spring than in any other season of the year. Rickets itself is probably not hereditary, but ill health in the parents undoubtedly predisposes to it. While congenital syphilis is not an etiologic factor, as Parrot believed, it may, like any other exhausting disease, incline a child to become rickety. There seems to be a general agreement that a defective diet is the essential factor, but whether the symptoms are due to a lack of some specific substance or to unfavorable proportions among the well recognized constituents of the diet is not clear.

Today attention is centered on the rôle of vitamins in relation to the etiology of rickets and many regard it as an established fact that a deficiency of the fat soluble vitamin, which is present in milk fat and to a greater extent in certain other fats, especially cod-liver oil, is the essential cause of the disease. On the other hand, Sherman and Pappenheimer[1] and Shipley, Park, McCollum, and Simmonds[2] believe that a deficiency in the phosphate ion may be the determining factor, the latter[3] concluding, however, from the results of a large number of experiments, that a disturbance in the physiologic relation in the diet between phosphate and calcium is of greater importance than the absolute amount of the salts themselves and may produce the rachitic complex in the absence of an organic substance contained in cod-liver oil sufficient to prevent it.

**Morbid Anatomy.**—The bones are thickened, especially in the region of the epiphyses, and lacking in normal consistence. Chemically they contain less mineral matter. If a section be made of a long bone it is found that the cartilage, periosteum, marrow, and bony tissue itself are congested; that the cartilaginous zone is very broad, irregular and bluish; that the line of ossification, instead of being straight and well defined, is wavy or irregular, poorly marked, and imperfectly calcified; that the end of the diaphysis is irregularly thickened and expanded; that the medullary spaces at the lines of ossification are unusually wide and the medullary canal is perhaps dilated; and that the marrow itself is more fibrous than normal. The changes in developing bones consist, therefore, of increased vascularity, excessive production of osteoid tissue both by osteoblasts and also apparently by metaplasia of the

[1] Proc. Soc. Exper. Biol. and Med., 1921, xviii, 193.
[2] Bull. Johns Hopkins Hosp., 1921, xxxii, 160.
[3] Jour. Biol. Chem., 1921, xlvii, 507.

cartilage, delayed and irregular calcification, and resorption of bone that is already formed in excess of the production of new osseous tissue. These changes make the bones less resistant to the traction of the muscles, the weight of the body and outside pressure, and consequently lead to bending, infraction, and marked deformity. Similar changes occur in the flat bones, and the result is abnormal thickening or thinning, according as overproduction of osteoid tissue or increased resorption is the dominant feature.

With recovery in rickets the bones become ossified and hard, but, as a rule, they remain deformed.

In addition to the osseous changes, the ligaments are lax, the muscles are atonic, and the spleen and liver are often enlarged.

The **pathogenesis** of rickets is still obscure. It is conceivable that the defective calcification may be due to some specific disturbance of calcium metabolism or to the inability of the osteoblasts to take up lime salts. During the florid stage of the disease the output of calcium in the feces is abnormally large, while the amount excreted in the urine is relatively small (Schabad and Dippelt). According to Howland and Kramer[1] the calcium content of the blood may be normal or slightly reduced, but the inorganic phosphorus of the serum is regularly low and the deficiency of the latter renders more difficult the precipitation of the tertiary calcium phosphate characteristic of bone.

**Symptoms.**—Rickets develops insidiously and in the majority of cases the possibility of the disease is first suggested by the *general disturbances* rather than by the skeletal changes. Some of the earliest symptoms are languor, fretfulness, excessive sweating about the head and neck during sleep, great restlessness at night and a constant habit of throwing off the bed clothes. Another symptom which often attracts the mother's attention is the child's disinclination to be moved or if he is lying on the bed or sitting on the floor to use his limbs. He may or may not be thin or anemic, except in long-standing cases with complications, but in any case his muscles are soft and flabby and he is easily tired. Often he has difficulty in sitting erect and almost invariably he is backward in walking. General hyperesthesia is frequent, as shown by the child crying when handled or moved. Extreme tenderness, however, is more suggestive of scurvy than of rickets. Occasionally the immobility of the limbs resulting from the hyperesthesia and impaired nutrition of the muscles is so pronounced as to suggest paralysis. Digestion is almost always deranged, and, owing to flatulent distention of the intestines, weakness of the abdominal musculature and diminished capacity of the thorax, "pot-belly" is very common. The spleen may show no change, but in many cases it is moderately enlarged and occasionally there is a veritable splenic tumor. In the absence of complications, the disease is afebrile. Mental development is, as a rule, not influenced by rickets.

The *changes in the osseous system* are the only pathognomonic features of the disease. In many cases the head is relatively large and more or less square in outline. The frontal or parietal eminences are often unduly prominent. The fontanelles and sutures remain open abnormally late. The anterior fontanelle, especially, instead of closing about the fifteenth month, may be open until the second year or even later. A groove-like depression dividing the skull longitudinally or transversely is occasionally seen. The cranial bones are often abnormally thick in some places and abnormally thin in others, and sometimes there are small areas which are actually soft and pliant (craniotabes). Delay or irregularity in the eruption of the teeth is very common.

[1] Amer. Jour. Dis. of Child., 1921, xxii, 105.

The changes in the ribs are especially characteristic. Besides the softening of the bones, which leads to flattening of the sides and sometimes to the deformity known as "pigeon-breast," the costochondral junctions are swollen so as to form a series of knobs extending from above downward and outward on each side of the chest. This constitutes the well known "rachitic rosary." There may also be a horizontal furrow at the base of the chest (Harrison's groove), marking the insertion of the diaphragm to the ribs.

The spine is not always affected, but not infrequently softening of the vertebræ leads to various deformities, the most common of which is kyphosis in the dorsō-lumbar region. The long bones usually show early deformity, the most notable changes being marked enlargement of the epiphyses, especially at the wrists and ankles, and bow-legs. Knock-knee and flat-foot are also common. In the pelvis the rachitic process is often followed by an increased projection of the sacral promitory with shortening of the conjugate diameter—a deformity in the female of preëminent obstetric importance. Severe rickets, especially if it occurs at an early period, sometimes interferes with the growth of bone and results in a subnormal stature (rickety dwarfism).

The x-ray picture is usually definite, the characteristic findings being increased permeability of the bones, and an irregular epiphyseal line with flaring out and cupping of the epiphyseal end of the diaphysis.

**Complications.**—Rachitic children are especially prone to catarrhal affections of the respiratory and digestive tracts. *Bronchitis* is very common, and owing to the general depravity of nutrition, feebleness of the respiratory muscles and thoracic deformities it is likely to become chronic or to extend into the finer bronchi and set up *bronchopneumonia*, which in rickets is an extremely dangerous disease. *Gastro-intestinal disorders* are also frequent and may be of any type and of any degree of severity. Rickety children almost invariably show some indication of abnormal nervous irritability, and not a few of them present *spasmophilic symptoms* in the form of recurring convulsions, laryngismus stridulus, tetany, or head nodding with nystagmus (spasmus nutans). Probably both the rickets and the spasmophilia are in some way connected with disturbed calcium metabolism. As other evidences of instability of the nervous system, *night terrors* (pavor nocturnus) and *nocturnal enuresis* may also occur. The most common complication on the part of the osseous system is the so-called *greenstick fracture*, which may be produced by comparatively little force. It may occur in any of the long bones, including the ribs and clavicles.

**Course and Prognosis.**—Although rickets runs a chronic course, it tends to subside spontaneously at the end of a year or two, and under appropriate treatment its active symptoms may cease entirely within a few months. It is not in itself a fatal malady, and yet its frequent complications make it a menace to life. With recovery the normal shape of the bones is sometimes regained, although marked deformities are likely to be permanent. Occasionally, however, even such pronounced changes as bow-legs and knock-knees seem to disappear spontaneously in the course of time.

**Diagnosis.**—When fully developed rickets can scarcely be overlooked. The only doubt is in the early stages. Head sweating and restlessness at night, delay in standing, in walking or in dentition, recurring bronchial catarrh, and spasmophilic conditions in children between the ages of 6 months and 2 years should excite suspicion and lead to a careful search for the characteristic physical signs. *Syphilitic epiphysitis* with *pseudoparalysis* is sometimes closely simulated, but this condition is usually seen between the fifth and twelfth weeks of life, and is accompanied by other evidences of

hereditary syphilis. Moreover, luetic pseudoparalysis shows a preference for the upper extremities and is, as a rule, more complete than that of rickets. Finally, in syphilis the x-ray shows localized areas of destruction in the diaphysis and usually marked periostitis, but no saucer-like expansion of the diaphysis.

In *infantile scurvy*, with which rickets is sometimes confused, the swelling is in the diaphysis and not in the epiphysis, the tenderness is often extreme, there are no changes in the cranium and none, as a rule, in the ribs, hemorrhages are common, if the teeth have been cut the gums are likely to be swollen and to bleed easily, and on x-ray examination the epiphyseal line is found to be intact, no saucer-shape expansion of the end of the diaphysis is observed but signs of subperiosteal hemorrhage are often present. *Achondroplasia* and *osteogenesis imperfecta* (fragilitas ossium) may sometimes come into consideration. In achondroplasia the lesions are congenital and permanent, teething and walking are not delayed, the nose is broad and flat, the head is usually globular, the extremities are abnormally short but the chest and trunk are normal or nearly so, the bones are dense and hard, and there is no predisposition to fractures. In osteogenesis imperfecta the chief feature is abnormal brittleness of the bones with recurring fractures. Digestive and nervous disturbances are wanting, the epiphyses are not enlarged, and there is no beading of the ribs. It is scarcely likely that *hydrocephalus* will be mistaken for rickets, as the head is regularly enlarged and rounded, the fontanelles are not rarely tense and bulging, intelligence is often impaired, and the thorax and extremities do not present the peculiar stigmata of rickets.

**Treatment.**—Measures intended to promote the mother's health during the procreative period, good hygienic surroundings, and proper feeding are the important factors in prophylaxis. If the mother be deemed unfit for nursing and a suitable wet-nurse cannot be procured, the diet must be given first attention. As a rule, clean, fresh unboiled cow's milk, properly modified to suit the age and digestive powers of the infant is the best food. After the first six months beef juice and egg albumin may be added. Proprietary foods, if used at all, should be limited to periods of emergency. A small amount of fresh orange-juice seems to be of service in some cases, even in the absence of any scorbutic taint. According to Hess,[1] it is feasible to rid a locality of rickets by the systematic use of cod-liver oil. After the first year eggs, scraped beef and stale bread with butter should, as a rule, form a fairly large part of the diet. Foods rich in starch must always be used sparingly, especially if there is much abdominal distention.

Next to feeding, general hygienic measures are of the most importance. An abundance of fresh air and sunshine are always to be recommended, but precautions against chilling must not be neglected. A tepid bath (about 85° F. at 6 months) should be given once a day in a warm room and followed by friction of the surface or very gentle massage. In regard to drugs, cod-liver oil not only benefits nutrition, but it definitely increases the capacity of the bones to take up or retain calcium. Phosphorus has also been well recommended, especially in combination with cod-liver oil. The phosphorated oil, each minim of which represents $\frac{1}{100}$ grain (0.00064 gm.), may be given in doses of $\frac{1}{2}$ to 1 drop, three times a day. Remedies to correct faulty digestion are often required, and in anemic cases, iron, preferably in organic form, is clearly indicated. To avoid deformities, sitting up, standing and walking should be discouraged while the bones are soft. For the same reason the child should not be carried always on the same arm or allowed to lie continuously on one side.

[1] Jour. Amer. Med. Assoc., 1921, lxxvi, 693.

## SCURVY

(Scorbutus)

**Definition.**—Scurvy is a disorder of nutrition due to defective diet and characterized by weakness, anemia, swollen spongy gums, and a tendency to hemorrhages.

**Etiology.**—Until the middle of the nineteenth century scurvy was very prevalent among sailors, soldiers, prisoners and others deprived for a long time of fresh food, but through a better insight into its causes, the use of suitable rations, and the observation of certain sanitary measures it has been almost completely stamped out among civilized peoples, at least as a disease of adults; nevertheless cases are occasionally observed among the poor, especially among the inmates of asylums, prisons, etc. and in persons who for one reason or another have been living for long periods upon inappropriate food. Bad hygienic surroundings, overwork, exposure to cold and wet and despondency favor the development of scurvy, but the essential etiologic factor is a deficiency in the variety of food, especially the prolonged lack of adequate quantities of succulent vegetables and fruits. Diets of cereals or legumes alone, or with meat, are apparently incapable of preventing it.

Although the disease is comparatively rare in adults at the present time, it is not very uncommon in infants, between the ages of six and fourteen months, who have been fed exclusively on certain artificial foods. This form of scurvy, which for a long time was regarded as "acute rickets," was first identified in 1878 by Cheadle,[1] and first fully described in 1883 by Barlow.[2] In Europe it is frequently referred to as *Barlow's disease.* It is most commonly produced by long-continued feeding on condensed milk, sterilized milk, pasteurized milk, or one of the proprietary foods, but raw milk and even breast milk of poor quality have been known to cause it.

How a defective diet operates to produce scurvy is still undetermined. It is generally conceded, however, that the fault lies in the lack of some accessory food factor, or vitamin, probably the water-soluble vitamin C., which is essential for normal nutrition. Infection seems to play a part, although only a secondary one, in producing some of the manifestations.

**Morbid Anatomy.**—The only constant lesion in adults is the occurrence of hemorrhagic extravasations, circumscribed or diffuse, in various parts of the body, as in and beneath the skin and mucous and serous membranes, under the periosteum, into and between the muscles, and into the joints and serous sacs. The hemorrhages are probably due to changes in the vessel walls. (Bierich[3]). The coagulability of the blood is about normal. The spleen is often enlarged, and the liver, heart and kidneys may be the seat of parenchymatous or fatty degeneration.

In *infantile scurvy* hemorrhages also occur, those about the bones being the most characteristic. The bones themselves show definite changes. The bone-marrow loses its lymphoid character and is poor in cells. Atrophy of the bone is sometimes observed, and in the large majority of cases a narrow zone of diminished density or of localized destruction is found just behind the epiphysis. As Fränkel[4] first pointed out, this zone appears in the x-ray plates as a characteristic white line. According to Erdheim,[5] the heart is almost always enlarged.

[1] Lancet, Nov. 16, 1878.
[2] Trans. Roy. Med. and Chirurg. Soc. 1, xvi, 1883.
[3] Deutsch. Arch. f. klin Med., 1919, cxxx, 151.
[4] Fortsch. ans. d. Gebiete der Röntgen., 1906, x, 1.
[5] Ueber das Barlowherz, Wien. klin. Woch., 1918, p. 1293.

**Symptoms in Adults.**—Scurvy sets in insidiously with general failure of health and strength, anemia, mental apathy and depression, and more or less severe pains in the limbs and joints, especially after exertion. With a continuance of the etiologic factors the debility increases, the complexion assumes a dirty-yellowish hue, and the anemia becomes pronounced, causing edema of the legs, dyspnea on exertion, palpitation, and a tendency to syncope. Sooner or later in the progress of the disease, hemorrhages in the form of petechiæ or ecchymoses occur in the skin and subcutaneous tissue. These appear first, as a rule, on the legs and then extend to the arms and trunk. Sometimes the extravasations result in the formation of blebs or are followed by a breaking down of the tissues and ulceration. In addition to these superficial hemorrhages blood may be poured out in the deeper tissues, giving rise to brawny tender swellings or indurations. Extravasations of this nature may occur in the calves, thighs, abdominal wall, popliteal space, over the tibia or elsewhere. Or bleeding may occur into the conjunctiva, into some of the joints, into the pleura or pericardium, or from one or another of the mucous membranes.

Of all the symptoms, however, the most characteristic are those afforded by the mouth The gums, especially around carious teeth, are swollen, dark and spongy, and bleed freely upon the slightest touch. They may even become purple or blackish, and rise above the level of the teeth as turgid, fungous growths. Loosening of the teeth and ulceration of the gums sometimes ensue and the breath has an intensely fetid odor. Mastication is painful and not rarely impossible.

Constipation is the rule, but diarrhea with offensive and bloody evacuations sometimes supervenes. In the absence of complications, the temperature is usually normal. The blood presents merely the changes of a secondary anemia. Night blindness (nyctalopia) is an occasional symptom.

In fatal cases death may be due to exhaustion, sudden syncope, hemorrhage into the cerebral meninges or to some intercurrent disease, such as colitis, pneumonia, or gangrene of the lung.

**Symptoms in Infants.**—In three-fourths of the cases infantile scurvy begins in the latter half of the first year of life. The disease is rare after the second year. The earliest manifestations are, as a rule, a gradual loss of color, diminished appetite, fretfulness, a reddish or purplish line of discoloration on the free edge of the gums, and especially pain or tenderness in the legs on movement or pressure. Hematuria is also an early feature in many cases. The blood may discolor the urine or it may be present in such small amount that it can be recognized only by microscopic examination. Occasionally close examination reveals a petechial spot on the hard palate, frenum of the tongue, gums, palpebral conjunctiva or here and there on the surface of the body. The child at first is usually well nourished, but soon he ceases to gain in weight. A pronounced increase in the rate of the pulse and respiration is not uncommon, even at an early period.

As the disease progresses the symptoms become more characteristic. Swelling accompanied by extreme tenderness about the diaphyses of the bones, most often about the lower portion of the tibia or femur, is frequently observed. This condition is the result of periostitis or subperiosteal hemorrhage. Equally characteristic is a pseudoparalysis of the affected limbs, most frequently the legs, which lie motionless and everted, usually with the thighs flexed and the knees slightly bent. In severe cases handling may reveal crepitus, which is due to the separation of the epiphysis by hemorrhage. The gums are not rarely injected and of bluish-red color, but unless the teeth have erupted they are not usually swollen and spongy, as in scurvy of adults. In

addition to the swelling about the diaphyses, simple edema is sometimes seen in the eyelids, feet or legs. Ecchymosis of the eyelid and protrusion of the eyeball (proptosis or exophthalmos) from an effusion of blood into the orbit are fairly common, but subcutaneous hemorrhages and bleeding from the mucous membranes are much less likely to occur than in adults. Hematomas, however, are occasionally seen over the cranium, scapula, ribs or elsewhere. The temperature is usually normal, but fever is sometimes observed in acute cases. Roentgenograms usually show the characteristic "white line" of Fränkel and frequently evidences of subperiosteal hemorrhage.

Indications of rickets not rarely accompany the manifestations of infantile scurvy, as the dietetic conditions that predispose to the one disease also favor the occurrence of the other. Gastro-intestinal disturbances and bronchopneumonia sometimes occur as complications, but are less common than in rickets. Pyelitis or pyelonephritis is also occasionally observed.

**Diagnosis.**—*Purpura* is the only disease with which scurvy of adults is likely to be confused, but purpura is not etiologically associated with dietetic errors and is not characterized by swollen spongy gums. Purpura hemorrhagica is further distinguished by the marked decrease in the number of blood-platelets.

Infantile scurvy may be mistaken for rickets, syphilitic epiphysitis, acute poliomyelitis, sarcoma of the bones, and especially rheumatism. The diagnosis from *rickets* is considered on p. 344. *Syphilitic epiphysitis* usually develops within the first three months of life, is accompanied by other evidences of syphilis, shows a predilection for the upper extremities, and lacks the tendency to hemorrhages and to tumefaction of the gums. Moreover in syphilis the x-ray does not show the white line behind the epiphysis or subperiosteal hemorrhages, but it does show, as a rule, areas of destruction and pronounced periostitis. In *poliomyelitis* the paralysis is complete, there is no swelling near the epiphysis, tenderness, if present, is usually much less than in scurvy, hemorrhages and changes in the gums are wanting, and the x-ray picture of the bones and joints reveals nothing abnormal. In *sarcoma* there is not necessarily a history of defective feeding, the swelling and tenderness are usually confined to one member, as the femur, hemorrhages and changes in the gums are absent, and the white line of Fränkel is not seen in the roentgenogram. *Rheumatism* is rare in children under two years of age and almost unknown in infants under one year of age, it produces swelling and tenderness in the joints rather than about the bony shafts, and is much more frequently accompanied by fever and local heat than scurvy. In all doubtful cases the therapeutic test should be applied, a change of diet always effecting a rapid improvement if the disease is scurvy. This is especially important, as there are many latent cases in which the only manifestations are pallor, anorexia, stationary growth, tachycardia and, perhaps, microscopic hematuria.

**Prognosis.**—Except in very severe cases and in those with complications, the prognosis is good under appropriate treatment. Improvement occurs with remarkable rapidity, although in some cases in adults weeks or months may pass before the patient's health is completely restored.

In *infantile scurvy* a suitable diet produces marked improvement within a few days and a cure usually within 2 or 3 weeks. If not treated, however, the disease may prove fatal through exhaustion, diarrhea, or pneumonia. Permanent disability or deformity of the limbs is exceedingly rare.

**Treatment.**—Scurvy can be completely prevented by observing proper hygienic measures and by the eating of a sufficient quantity of fresh food. For

use on shipboard, in camps, etc. potatoes, onions, beets, cabbage and certain fruits, particularly lemons, limes, or oranges, are valuable antiscorbutics. Generally speaking, heating, desiccation and oxidation lessen or destroy the antiscorbutic vitamin; nevertheless canned tomatoes, dried orange juice or tomato juice, and milk that has been dried by being subjected to a temperature of 230° F. for only a few seconds possess considerably antiscorbutic potency. Pasteurization of milk apparently produces greater deterioration than boiling for a few minutes.

When scurvy has already developed rest and an abundance of fresh air and sunlight are important adjuvants to the dietetic treatment, which consists in giving generous amounts of fresh meat and fresh vegetables with several ounces of lemon, lime or orange juice daily. If the patient is unable to chew, owing to severe gingivitis, the diet must be limited to fresh milk, eggs, strong animal broths, purée of potatoes and fruit juices. Drugs are of secondary importance, although iron and bitter tonics, especially quinin, are often of value. The affected gums should be painted with a solution of silver nitrate—10 grains to the ounce (0.65 gm. to 30.0 mils)—and the mouth should be washed at frequent intervals with a solution of potassium permanganate or potassium chlorate.

*Infantile Scurvy.*—In artificially fed infants scurvy can be prevented by using raw milk of good quality and suitably modified to the exclusion of heated milk and proprietary foods. If pasteurized milk must be used the child should be given orange juice (1 tablespoonful daily) after the first month. In the treatment of the disease orange juice is a specific. The dose is from 1 to 2 tablespoonfuls daily. Purée of potato is also useful and may be substituted for the orange juice if there is diarrhea. Cod-liver oil and yeast have no antiscorbutic potency. The painful limbs should be kept warm.

## BERIBERI

### (Kakke)

**Definition.**—Beriberi,[1] is an acute, subacute or chronic disease, caused by a deficiency of certain accessory food substances, and characterized anatomically by degeneration of the peripheral nerves, and clinically by various sensorimotor disturbances, irritability and weakness of the heart, and more or less edema.

**Etiology.**—Beriberi has been known in the Orient from time immemorial. Only since the latter part of the last century, however, has it been clearly recognized that the chief anatomical change in the disease is a degeneration of the peripheral nerves, and only within the last decade has it been definitely established by the researches of Fraser and Stanton,[2] Strong and Crowell,[3] Chamberlain and Vedder,[4] Funk,[5] McCollum and Davis,[6] and others that the essential etiologic factor in beriberi is too exclusive feeding on over-

[1] *Beri* is Singhalese for weakness; *Kakke* is from the Chinese *kiaku*, legs and *ke*, disease.
[2] Studies from the Institute for Med. Research, 1909, No. 10; 1911, No. 12.
[3] Philippine Jour. Sci., 1912, vii.
[4] Philippine Jour. Sci., 1911, vi.
[5] Jour. of Physiol., 1911, xliii, 26 and 1912, xlv.
[6] Jour. Biol. Chemistry, 1915, xxiii.

milled or highly polished rice or on other carbohydrate food which is deficient in so-called antineuritic vitamin.[1]

Recent studies tend to show that the vitamin is concerned in some way with carbohydrate metabolism and that the larger the amount of carbohydrate consumed the greater the demand of the organism in respect of the essential substance. A liberal variety in diet, however, lessens considerably the chance of deficiency.

Beriberi has been endemic principally in Japan, China, the Dutch East Indies, Malay Peninsula, the Philippine Islands and India, but it has been prevalent at times in Brazil and on the east and west coasts of Africa, and occasionally it has appeared in England and in America. Heat and moisture are favorable to outbreaks, hence in climates with cold and hot months, the disease usually prevails during the latter and when there are dry and rainy seasons it most frequently occurs in the rainy one. Overcrowding, foul air and physical exhaustion are auxilliary etiologic factors, consequently in endemic regions the poor suffer in greater proportion than the rich, and for the same reason many of the worst outbreaks have occurred in barracks, asylums, jails and ships. In two years of the Russo-Japanese war more than 80,000 Japanese soldiers were incapacitated by the disease. The majority of cases occur in young adults, but no age is exempt. Even infants who are nourished by beriberi mothers are sometimes affected. In the Philippines the disease is largely responsible for the excessive infant mortality. Males suffer in larger numbers than females.

**Morbid Anatomy.**—In many cases the subcutaneous tissue is edematous and the serous sacs contain an excess of straw-colored fluid. Petechiæ are sometimes seen beneath the serous membranes. The heart, particularly the right ventricle, is usually much enlarged. The myocardium is flabby and mottled, in consequence of fatty changes. The veins are, as a rule, engorged. The lungs are congested and edematous. The liver is congested and swollen and microscopically exhibits varying degrees of cloudy swelling and fatty degeneration. The spleen and kidneys, beyond being somewhat hyperemic, show no marked change. Inflammatory lesions are almost constantly present in the stomach and duodenum. Except in the most rapidly fatal cases, microscopic examination of the peripheral nerves, particularly of the vagi and those of the lower extremities, reveals the usual evidences of parenchymatous degeneration. As in other forms of polyneuritis changes may also be observed in the anterior-horn cells and posterior columns of the spinal cord. The muscles supplied by the affected nerves present the appearances of a degenerative atrophy.

**Symptoms.**—Clinically, the manifestations of beriberi are those of a multiple neuritis with marked involvement of the pneumogastric and vasomotor nerves. The attack is usually ushered in with malaise, symptoms of indigestion, and a feeling of heaviness in the legs. Neuritic features follow in from a few hours to two or three days. These include flaccid paresis, especially of the lower extremities, sensitiveness of the nerve-trunks to

[1] It is known today that there are at least three vitamins—one soluble in fat (Fat Soluble A), and the other two soluble in water (Water Soluble B and Water Soluble C). The water soluble vitamins structurally resemble the purins, and the fat soluble vitamin is closely related to lipoids. Fat Soluble A, which is apparently antirachitic, is present in animal fats, various meats and many vegetables. Water Soluble C, which is anti-scorbutic, is present in fresh vegetables and to some extent in fresh meats. Water Soluble B, which is antineuritic, is found more or less abundantly in the germ and bran layers of cereals, in peas, beans, carrots and potatoes, in nuts, in brewers' yeast, in milk, in eggs, and in various meats. A temperature of 212° F. (100° C.) does not seriously impair vitamins, but a temperature between 250° and 270° F. (66°–120° C.), especially if long continued, destroys them.

pressure, muscular soreness, paresthesia, and hypesthesia. The tendon reflexes are soon diminished or abolished, although at first they may be exaggerated. Muscular atrophy supervenes and in protracted cases becomes very conspicuous. Edema, varying in degree from slight pretibial swelling to pronounced anasarca, is nearly always present. Symptoms of cardiac irritability and insufficiency are also very common. In mild attacks there may be merely palpitation on slight exertion, precordial discomfort, and a frequent, ill-sustained pulse, but in grave, rapidly fatal cases there are all the evidences of extreme dilatation of the heart with resulting venous engorgement. Even when the heart is not especially weak, dyspnea may be urgent owing to accumulations of fluid in the thoracic cavities or to paresis of the respiratory muscles. The mind is usually clear, although exceptionally psychic disturbances similar to those of alcoholic neuritis (Korsakow's syndrome) are observed. In the absence of complications, the temperature is either normal or very slightly elevated.

**Varieties.**—*Acute pernicious cases* are met with in which symptoms of cardiac exhaustion and dilatation develop with alarming rapidity and death occurs within a day or two. On the other hand, extremely mild attacks are observed in which the only symptoms are malaise, weakness in the legs, and slight irritability of the heart (*abortive form*). The majority of cases are acute or subacute, lasting from three to eight weeks. In some of these the sensorimotor disturbances dominate the picture, edema being slight or absent (*dry beriberi*); in others, dropsy is the conspicuous feature, the vasomotor system apparently bearing the brunt of the poison (*wet beriberi*). Recovery is the rule in both the dry and wet forms, nevertheless, many patients die from heart failure, asphyxia, or exhaustion, and many others gradually pass into a chronic condition (*beriberi residual paralysis*) with atrophic paresis of the limbs and a more or less crippled heart.

**Diagnosis.**—Beriberi can be distinguished from other forms of polyneuritis only by the peculiar circumstances under which it develops and the marked tendency of the process to involve the heart and to excite edema. *Scurvy*, which is also a deficiency disease, may be differentiated by the presence of swollen, spongy bleeding gums and of hemorrhages into the subcutaneous tissues, and by the absence of paresis. In *famine edema*, or "*war dropsy*," which is apparently due to a diet deficient in total calories, combined with excessive fluid and salt intake, there are no typical polyneuritic symptoms, polyuria is somewhat frequent, and so is dimness of vision from opacity of the cornea (xerophthalmia), this last probably depending upon a lack of the fat-soluble vitamin.[1]

**Prognosis.**—The mortality varies with the character of the outbreak, the physical stamina of the persons attacked, and their environment. It may be as high as 50 per cent. or as low as 2 per cent. In individual cases the prognosis should always be guarded, for even in attacks that are apparently mild grave cardiac symptoms may arise suddenly at almost any period of the disease.

**Prophylaxis and Treatment.**—Beriberi is a preventable disease. Important prophylactic measures are the supply of as liberal variety in diet as possible, the substitution of brown, undermilled rice for polished rice, of whole wheat flour for white wheat flour, and of yellow or water-ground cornmeal for white cornmeal, the addition of barley to all soups, and the use of fresh vegetables or fruit, white potatoes and fresh meat at least once a week. Canned foods and meats that have been subjected to prolonged boiling are without prophylactic value.

[1] For a full description of famine edema, see article by Maver, Jour. Amer. Med. Assoc., April 3, 1920, p. 934.

The chief therapeutic indication is to supply foods rich in antineuritic vitamin. Raw milk, eggs, rare beef juice, barley soup, yeast, extract of rice polishings and malt extract are especially valuable. Absolute rest in bed is essential, even in the mildest cases. For the edema simple diuretics are recommended. In the event of cardiac dilatation digitalis, caffein, strophanthin (intramuscularly) and camphor (subcutaneously) are the best drugs. Venesection has been employed with encouraging results in some instances. In beriberi residual paralysis, massage, electrical stimulation, etc. are required, as in other forms of chronic neuritis.

## PELLAGRA

**Definition.**—Pellagra[1] is a chronic endemic disease, characterized by a complexity of cutaneous, gastrointestinal and nervous symptoms, with seasonal exacerbations and remissions, and a tendency to terminate in dementia and exhaustion. It was first accurately described by a Spanish physician, Gaspar Casal, in 1735, and the name pellagra was given to it by the people of Northern Italy, among whom the disease has prevailed extensively for many years.

**Etiology.**—Pellagra is common in Southern Europe, Egypt, India, Central America and the West Indian Islands. In this country it is especially widespread in the Southern States, although cases have been reported from nearly every state in the union. The number of pellagrins in the Southern States has been variously estimated from 50,000 to 150,000. Poverty and poor hygienic conditions are predisposing factors. No age is exempt, but the greatest incidence is between the second and fifth decades. Females are affected more frequently than males. White and colored races seem to be equally susceptible. Although multiple cases are frequently observed in a single household, there is no evidence that pellagra is either hereditary or contagious.

The cause of pellagra is unknown. According to one view, the zeistic view, the disease is due to a preponderance of maize or the use of spoiled maize, such food being insufficient or inappropriate, or, perhaps, containing some toxic substance or being the carrier of some form of parasite. According to another view pellagra is an infectious disease due to a specific organism, which as yet has not been isolated. A third view places it, along with scurvy and beriberi, among the "food deficiency diseases" and ascribes it to a lack of some essential dietary substance or vitamin. More recently the hypothesis has been advanced that pellagra is due to the absorption of toxic products originating in the intestinal tract and related to an altered flora, which in turn is brought about by a deficiency of certain foods or by unfavorable proportions among well recognized constituents of the diet. The weight of evidence favors the view that pellagra is a nutritional disease resulting from a lack of proper food balance.

**Morbid Anatomy.**—The visceral lesions are mostly of an atrophic and degenerative nature, and suggest a chronic intoxication rather than an infection. Varying degrees of degeneration are commonly found in the ganglion cells of the brain and spinal cord and not rarely also in the posterior and postero-lateral columns of the spinal cord, the latter being most marked, as a rule, in the lumbar and cervical regions.

[1] Ital., *pella*, skin; *agra*, rough.

**Symptoms.**—The more obvious manifestations of pellagra usually appear first in the spring, although they are almost always preceded for weeks or even months by less pronounced disturbances consisting of lassitude, muscular weakness, vertigo, headache, epigastric discomfort, flatulence and pyrosis. When fully developed the disease is characterized by marked derangements of digestion, especially recurring diarrhea, a peculiar erythematosquamous skin eruption, which affects chiefly the exposed parts of the body, and various nervous phenomena, which in the later stages, at least, are indicative of degenerative changes in the spinal cord and cerebrum. An important feature of the disease is the tendency of the exanthem and gastrointestinal symptoms to recur every spring or summer during a period of years and to remit, or perhaps completely disappear, in the winter months. In the later stages the patient becomes greatly emaciated, exhausted, and not rarely completely demented. While the disease is for the most part afebrile, there is sometimes moderate fever with mild delirium (*pellagra typhoid*) during acute exacerbations and toward the close of life. The blood changes are those of secondary anemia and have no diagnostic value.

In America the disease is gradually becoming less prevalent and less severe and cases without an eruption are more frequently observed than formerly.

The *gastro-intestinal symptoms* appear early and often prove intractable. The tongue at first has a flabby appearance, with central furring and red tip and edges; later it loses its epithelium and becomes bare and red. Salivation frequently accompanies the stomatitis. Vomiting is not uncommon, and recurring diarrhea with watery or mucoid stools is almost a constant feature. Examination of the gastric contents not rarely shows a complete absence of free hydrochloric acid.

The *eruption* usually follows the gastro-intestinal disturbances, but it may appear simultaneously or be the first symptom to attract attention. It develops, as a rule, suddenly in the spring and is for the most part limited to areas that are commonly exposed to the sun, as the back of the hands, the face (pellagrous "mask"), and, in persons who go barefooted, the dorsal surfaces of the feet. A band about the neck (Casal's "collar") is also common. The lesions, which are symmetrical and sharply delimited, are at first of a dull red color, like a sunburn, and later of a peculiar reddish-brown hue. With the evolution of the disease the affected skin becomes tense and swollen, then thickened, rough and scaly, and finally atrophic. In some cases vesicles, bullæ, and petechiæ complicate the process. Subjectively there is burning rather than itching. In addition to the typical exanthem on the exposed parts, there are not rarely areas of erythema about the scrotum or the vulva. The tendency of the cutaneous lesions to disappear or recede in the winter and to recur in the spring is characteristic.

The *nervous symptoms* of the early stages consist chiefly of neurasthenia with melancholy moods, paresthesias, tremors and muscular cramps. The later symptoms are extremely varied. Usually profound mental depression with retardation of all the psychic functions is the dominant feature, but exaggeration of the tendon reflexes, ataxia and spastic paresis are also frequently found. In severe cases there may be hallucinations of sight and hearing, and delusions of a persecutory character. Rarely epileptiform and cataleptic seizures occur. In the final stages dementia or a condition simulating general paresis not rarely supervenes.

**Diagnosis.**—The diagnosis is usually not difficult except in the prodromal stage and in atypical or ill-defined cases occurring outside of the usual districts for the disease. It is based upon the recurrence each spring of a

sharply delimited, symmetrical, and pigmented erythematosquamous eruption in association with nervous symptoms and gastro-intestinal disturbances, especially diarrhea.

**Prognosis.**—In the early stages of the disease the outlook is good, if the conditions are favorable. Each recurring attack makes the prognosis more serious. The mortality in Italy is now less than 10 per cent.; in this country it is given as from 25 to 40 per cent., although these figures apply chiefly to advanced cases. The average duration is probably about 5 years, but acute cases lasting only a few months have been reported. Intermissions are not uncommon.

**Treatment.**—The brilliant results of the Italian campaign against pellagra have demonstrated the great value of good hygienic environment and a well balanced diet in prophylaxis. As to treatment, there is no specific remedy. A varied nutritious diet, removal to suitable hygienic surroundings, rest, and hydrotherapy are all important. The diet should include liberal amounts of milk, eggs, meat, bread and butter, and vegetables rich in protein, a caloric intake of at least 2500 being maintained, if possible. Drugs play a minor part in the treatment. Arsenic, in the form of Fowler's solution, sodium cacodylate or arsphenamin, and iron are sometimes of service. Tincture of nux vomica before meals is a useful stomachic. Persistent diarrhea is best combated by rest in bed, appropriate feeding, and the administration of dilute hydrochloric acid.

# DISORDERS OF METABOLISM

## GOUT

(Podagra)

**Definition.**—Gout[1] is a chronic disorder involving the disposition of the purin substances in the body and characterized by an excess of uric acid in the blood and in its typical form by a deposition of monosodium urate in the cartilages of the joints and in certain other structures and by recurring attacks of acute arthritis.

**Etiology.**—Gout is apparently more common in England than in America, although the studies of Futcher[2] and others indicate that it is less rare in America than has been supposed, not a few cases being mistaken for and treated as rheumatism. *Heredity* is probably the most important of the predisposing causes, more than fifty per cent. of the cases occurring in persons with a gouty ancestry. The disease most often develops in *middle life*, the first attacks usually occurring between the ages of thirty and forty-five years. It rarely begins in childhood or old age. Males suffer much more frequently than females. Great stress is laid upon the free use of *alcoholic drinks*, more particularly of fermented beverages, such as heavy wines, beer, ale and porter, as an etiologic factor, and from time immemorial sedentary habits, the excessive consumption of food, especially meat, and *luxurious living* in general have been regarded as being strongly conducive to the disease. Gout is not, however, the consequence only of ease and luxury; while it is undoubtedly more prevalent among the rich than the poor, it is by no means uncommon in the humbler walks of life, particularly among those who fare badly and consume large quantities of malt liquor. The influence of *chronic lead poisoning* in the production of gout is generally acknowledged. Garrod found that at least 25 per cent. of the gouty patients in his hospital practice at some period of their lives had been affected by lead. In Futcher's series of 54 cases admitted to the Johns Hopkins Hospital 6 patients were painters and 3 were tinners. It is possible that plumbism disposes to gout by interfering with the excretion of uric acid. The first attack of acute gout usually occurs in the winter season.

The paroxysms of acute gouty arthritis may be excited by a variety of causes, namely, overeating or drinking, violent or depressing emotions, sudden changes of temperature, mental or physical exhaustion, or local injury. The frequency with which the ball of the great toe is affected is explained by the fact that this joint is more exposed than any other to sprains and bruises.

**Pathogenesis.**—Uric acid is a derivative of the nucleoproteins (nucleic acid) of the body cells (*endogenous uric acid*) and of the nucleoproteins and free purin bodies[3] of food (*exogenous uric acid*). There is no evidence that uric acid is ever produced in human beings by synthesis from foods that

[1] The name *gout* is derived from the Latin *gutta*, a drop. and owes its origin to the ancient conception that the disease depended upon a peculiar noxa which fell drop by drop into the affected joint.

[2] Jour. Amer. Med. Assoc., Nov. 26, 1904.

[3] The purin bodies are all derivatives of the hypothetic compound, $C_5 H_4 N_4$, discovered by Emil Fischer and designated by him as "Purin." Caffein and theobromin belong to the same group and are capable of transformation into uric acid.

contain no purins. The excretion of endogenous uric acid by healthy human beings under fixed conditions is fairly constant for each individual. It is not markedly increased by vigorous physical exercise. The output of exogenous uric acid varies considerably with the amount of purin bodies taken in the food. When the proteins of the food contain many nuclei (sweetbread, liver, kidney, brain) the excretion of uric acid in the urine is distinctly increased. Flesh also increases the output of uric acid in the urine, for while it is poor in nucleoprotein it is comparatively rich in free purin (protoxanthin). On the other hand, proteins free from purin bodies, such as egg albumin and casein, do not increase the uric acid output. Of the total quantity of purin bodies in the urine about nine-tenths exists as uric acid and one-tenth as purin bases. The amount of uric acid eliminated daily in healthy adults ranges between 0.4 and 1.0 gram, from 0.15 to 0.40 gram per day being of endogenous origin.

The purin derivatives probably travel in the blood stream as nucleotids (complexes of purin, phosphoric acid and carbohydrate radicals) and as nucleosids (compounds of purin with sugar groups). The latter yield in the tissues uric acid, which, in turn, is promptly excreted. Hence, under normal conditions the uric acid is ordinarily kept at a low and fairly uniform level—1.5 to 2.5 mgs. in 100 c.c.—even when the diet is rich in purins. According to Gudzent uric acid ordinarily exists in the blood in two forms—one readily soluble (lactam form), the other relatively insoluble (lactim form).

The precipitation of uric-acid crystals or of urates from urine does not necessarily indicate, as was formerly supposed, an increased excretion of uric acid, since such a precipitation frequently occurs as a result of changes in the chemical composition of the urine. An actual increase of the uric acid of the urine can be determined only by quantitative methods. Furthermore, the quantity of uric acid in the urine is by no means an accurate index of the quantity in the blood. The urinary output varies not only with the amount of purin bodies taken with the food and the amount of destruction of tissue nucleoproteins, but also with the power of the kidneys to excrete uric acid and the capacity of the tissues to retain uric acid. Once formed in the body, however, uric acid is either excreted or retained, for the human organism does not possess the power of destroying it.

The theory that uric acid stands in direct relation to the symptoms of gout originated in the latter part of the eighteenth century, when Wollaston[1] made known the chemical composition of gouty concretions. It was materially strengthened fifty years later by the observation of Garrod[2] that the blood of gouty patients contains an abnormal amount of uric acid. Although this finding of Garrod has been fully confirmed by the researches of others, the cause of the excess of uric acid remains uncertain. It is conceivable that the condition may be due to increased formation or to decreased excretion. As there is not the slightest evidence of an overproduction of purin compounds in gout, interest has centered on the problem of elimination. It is generally believed that the excessive concentration of uric acid in the blood of gouty patients is due to impaired renal permeability, which results in a higher threshold for the excretion of uric acid. This functional incapacity of the kidneys, while it commonly occurs in cirrhotic nephritis, is not necessarily due to nephritis, for the amount of uric acid in the blood bears no relation to the amount of urea and total non-protein nitrogen. Other explanations of the high uric acid content of the blood in gout have been offered. Minkowski suggested that the lessened excretion of uric acid may

[1] Phil. Trans., London, vol. ii, 1797.
[2] Medico-Chirurg. Trans., vol. xxv.

be due to the existence of the purin in some abnormal union, and Umber has suggested that the uric acid accumulates in the blood not on account of any renal deficiency, but because it is actively retained by the tissues. Certainly an excess of uric acid in the blood does not alone account for the phenomena of gout for a pronounced excess occurs also in leukemia, chronic nephritis, plumbism and a number of other conditions.

For the deposition of monosodium urate in the cartilages of the joints no satisfactory explanation is at hand. Ebstein ascribed the precipitation to a primary necrosis of the tissues, but the researches of Freudweiler and His[1] and others have not supported this view. Roberts suggested that the richness of the articular cartilages in sodium chlorid may be a factor. Others have held the poor vascularity of the parts responsible, and others still have laid stress on the fact that the affected parts are especially exposed to cold. The cause of the arthritis in acute gout is also obscure. It is generally assumed that the inflammation is excited mechanically by the deposition of the urate crystals in the tissues, but this view does not harmonize with the fact that uratic concretions often attain a large size without causing any symptoms whatever. Uric acid is not especially toxic, and eventually it may be demonstrated that it is not the offending agent in gout, but merely an accompaniment of a more subtle poison—one also formed through faulty purin metabolism—that is the real cause of the lesions and symptoms.

**Morbid Anatomy.**—The joint lesions are characteristic. The conspicuous feature is the appearance of fine uratic crystals in the articular cartilages and later in the ligaments, the capsule, the synovial membrane and the adjacent tissues. In the course of time the uratic deposits grow by concretion into large white masses, known as *tophi*, producing more or less enlargement and deformity of the joint. Chemically, tophi consist principally of monosodium urate (sodium biurate), although calcium salts are also present in variable proportions. Very frequently each successive deposit of urate in a joint is marked by a severe inflammatory reaction (acute attack or "fit" of gout), which is manifested by hyperemia and edematous swelling of the tissues in and about the joint, and some increase in the quantity of synovial fluid. In certain localities, however, tophi form gradually without causing acute symptoms. In advanced cases secondary changes occur in the affected joints. The commonest of these is thickening of the capsular tissues. Sometimes, erosion of the cartilages also occurs. Occasionally the injured tissues become infected and in this event suppuration may ensue with rupture of the skin and the discharge of the uratic concretion. Tophi may also escape through the skin after it has undergone atrophy, through stretching, and may even disappear by absorption. The metatarsalphalangeal joints of the great toes are most frequently involved, but other small joints of the feet and hands, and even the wrists, ankles and knees are liable to be attacked. Tophaceous deposits may also be found in other tissues, such as the cartilages of the ear, various bursæ, the larynx, the eyelids, the subcutaneous tissue, and the kidneys.

Apart from the deposits of uric acid in the renal papillæ, there are no characteristic visceral changes, but cirrhosis of the kidneys, arteriosclerosis and hypertrophy of the heart with fibroid changes in the myocardium are common pathologic findings. Whether the renal and cardiovascular lesions are the direct result of the peculiar irritants produced in the gouty process or are merely concomitant conditions arising from the same causes that brought on the gout is not definitely known.

**Symptoms.** *Acute Gout.*—This phase of the disease manifests itself by an

[1] Deutsch. Arch. klin. Med. 1899, lxiii, 266.

acute inflammation of one of the smaller joints, usually the ball of the great toe. As a rule, the attack begins at night, especially in the early morning hours, the patient being suddenly aroused from sleep with violent articular pain of a boring, throbbing or burning character. Certain prodromal manifestations, such as indigestion with flatulence, muscular cramps, chilliness or irritability of temper often indicate the approach of a paroxysm, but at times, particularly in the first attack, the characteristic symptoms supervene without warning. The painful joint soon becomes swollen, of a vivid red color, and so exquisitely tender that the slightest jar causes intense distress. The skin over it is shiny and the superficial veins often appear full and distinct. Toward morning the pain usually abates to a considerable extent and the patient may fall asleep. During the day he is sometimes fairly comfortable, but every night for a period of several days his suffering returns, although with gradually diminishing severity. Not rarely ten days or two weeks elapse before the tenderness and swelling have entirely disappeared, and occasionally there is a succession of paroxysms lasting a month or longer. The subsidence of the inflammation is usually marked by itching of the part and desquamation of the cuticle.

The general symptoms accompanying these local phenomena are moderate fever (100°–101° F.), restlessness, chilliness, and more or less disturbance of digestion. Leucocytosis is sometimes observed. The excretion of uric acid in the urine is reduced just before an attack and is increased during an attack. Between the attacks it is usually about normal, although it may be diminished. After the acute symptoms have disappeared the patient often feels much better than he has done for weeks or months previously.

Recurrences are the rule. At first these take place at relatively long intervals, perhaps two or three years, then annually, and later every few months. As the disease progresses, the acute form tends to merge into the chronic form, each successive paroxysm becoming less characteristic and less severe, but lasting longer and involving an increasing number of joints and leaving behind a greater degree of stiffness and deformity.

*Chronic Gout.*—This phase is usually secondary to acute gout, but it may be primary. It is characterized by the formation of uratic concretions in various parts of the body, especially in and about the joints and in the pinnæ of the ears, by permanent thickening of the periarticular tissues, by frequent and irregular paroxysms, and by the development, sooner or later, of serious visceral lesions. The joints most frequently involved are the small ones of the feet and hands. Then come the knees, wrists, elbows and ankles. The shoulders, hips, sternoclavicular and temporomaxillary articulations are usually spared. As the disease progresses the affected joints become stiff, enlarged, lumpy and deformed, owing to the extensive accumulation of urates. These accumulations, or tophi, vary in size from a small shot to a filbert and are likely to be particularly numerous and prominent about the knuckles. Occasionally, the overlying skin ulcerates or becomes so stretched that it breaks, thus allowing the chalk-like concretions to escape. The paroxysms of chronic gout are accompanied by less febrile disturbance, occur more frequently, and last longer than those of the acute disease. Indeed, they not rarely overlap, a fresh attack appearing before the preceding one has completely subsided. The x-ray appearances of the joints in gout are not characteristic and in advanced cases may closely resemble those of proliferative arthritis deformans. The most constant changes are an increased permeability and a variable degree of atrophy of the bones with narrowing or disappearance of the joint-slits.

*Urinary Symptoms.*—In the early stages the urine is often strongly acid,

dark colored and of high specific gravity. On standing, it may show a crystalline sediment of uric acid. These features, however, are not constant in gout nor peculiar to it. On the whole the excretion of uric acid goes on within normal limits, except during acute exacerbations, when for several days it may rise somewhat above the average level. Late in the disease there is usually renal cirrhosis, the urine in consequence being copious, pale, of low specific gravity, and containing traces of albumin and hyaline and granular casts. That gout favors to some extent the occurrence of urinary calculi is generally acknowledged.

*The Blood.*—In the large majority of cases the blood, with the patient on a purin-free diet, shows an excess of uric acid, or more than 3 mg. per hundred c.c., when examined by the method of Folin and Denis. High figures for uric acid, however, are not pathognomonic of gout, since an excess also occurs in certain other conditions, notably leukemia, chronic nephritis, chronic lead-poisoning and acute infections, especially lobar pneumonia. On the other hand, a low figure for uric acid in the blood is strong evidence against gout.

*Digestive Disturbances.*—Gouty patients are prone to recurrent attacks of indigestion, with a sense of oppression in the epigastrium, foul breath, flatulence and irregular action of the bowels. Attacks of diarrhea may also occur. A deficiency of hydrochloric acid is not an uncommon finding. These disturbances are, of course, not characteristic of gout and are probably due to the habits of the patient rather than to the disease itself.

*Nervous Manifestations.*—Many patients suffer at times from headache, dizziness, loss of energy, both mental and physical, irritability of temper, and depression of spirits. Attacks of neuralgia or of migraine are not infrequent. Painful cramps in the muscles of the legs are somewhat common. Sciatica and other forms of neuritis are occasionally traceable to gout.

*Cardiovascular Features.*—Arteriosclerosis nearly always develops sooner or later, and generally in association with chronic nephritis, these two lesions constituting the two most common and serious sequels of gout. As a result of the vascular changes cardiac hypertrophy, myocardial disease, angina pectoris or apoplexy may also occur.

*Pulmonary Disorders.*—Chronic bronchitis is often observed in gouty subjects. Emphysema is likewise common.

*Cutaneous Affections.*—Certain skin diseases seem to have something more than an accidental relation to gout. This is especially true of eczema and psoriasis. Occasionally there is annoying pruritus. The capillaries of the face are frequently dilated and the nails may be longitudinally grooved or fluted.

*Ocular Manifestations.*—In rare instances conjunctivitis, iritis and glaucoma seem to owe their origin, either directly or indirectly, to gout. Garrod draws attention to the occurrence of uratic concretions in the sclera with inflammation of this coat of the eye.

*Other Anomalies of Metabolism.*—It is well established that a relation sometimes exists between gout and diabetes mellitus and between gout and obesity. All three of these conditions or any two of them may occur in the same individual, the habits of living that favor the development of the one also predisposing to the others.

**Irregular Gout (Masked, Larval or Latent Gout).**—These terms have been applied to a form of chronic gout, by no means uncommon, in which the general manifestations of the disease are well marked, but the articular symptoms are slight or altogether absent. It is generally observed in persons whose parents or grandparents have had gout, but undoubtedly it may be

acquired through a too free indulgence in the pleasures of the table and an indolent mode of living. The diagnosis is often difficult. In arriving at it one should always consider very carefully the family history, the habits of the patient, the whole range of symptoms, and the way that the last are influenced by diet and exercise. Not infrequently the occurrence of abortive paroxysms, indicated by slight swelling and tenderness of the joints, affords a valuable clue. In no case, however, should a symptom be attributed to gout merely because it happens to be associated with an occasional deposit of uric acid in the urine.

**Retrocedent Gout.**—This term is applied to certain serious internal disturbances occurring coincidentally with a rapid subsidence of the acute articular manifestations of gout. The patient may be suddenly seized in one case with acute abdominal pain, vomiting and diarrhea, in another case with a sense of precordial oppression, dyspnea and syncope, and in a third case with delirium, stupor and coma. The cause of these peculiar attacks is not always apparent. They have been ascribed to a form of metastasis, but it is probable, that in some instances, at least, they are really an expression of uremia or of angina pectoris.

**Diagnosis.**—This is usually not difficult in acute cases. The features by which *acute rheumatism* may be excluded have been considered in the description of that disease (see p. 253). Among other articular affections, *arthritis deformans* is the one most likely to be confused with gout. In arthritis deformans, however, inquiry into the family history, habits and occupation of the patient does not afford the important clue that it frequently does in gout; certain joints (hip-, shoulder-, vertebral, temporomaxillary and sternoclavicular joints) are commonly attacked that are usually spared in gout; the attacks usually develop less suddenly than in gout, and show no special tendency to begin in the early morning hours; the skin over the affected joints rarely presents the peculiar shiny redness that is so often seen in gout; the affected joints are, as a rule, more rapidly crippled and distorted than in gout; muscular atrophy is more common than in gout; tophi are never found in the ears, knuckles or elsewhere; the uric acid content of the blood is not usually above normal; and finally, the pulse rate is often persistently accelerated, which is not the case in gout.

**Prognosis.**—Acute gout rarely proves fatal. The first attack may also be the last, but this is exceptional, and even under the most favorable conditions recurrence is to be expected. The outlook in chronic gout depends largely upon the intensity of the constitutional vice and the extent to which the patient's habits of life can be controlled. Many gouty subjects live to a good old age; nevertheless, the disease, on the whole, tends to shorten life. The fatal issue is usually determined by uremia, cardiac insufficiency, angina pectoris, apoplexy, or intercurrent infection, especially pneumonia.

**Treatment.** *The Acute Attack.*—At the outset a brisk mercurial purgative, followed by a saline, is almost always advisable. The diet should be restricted to milk, eggs and farinaceous foods. The liberal use of water should be encouraged. Two drugs are especially efficacious, namely, colchicum and cinchophen (atophan). The former is used empirically; the virtue of the latter apparently depends upon its power to increase the excretion of uric acid. Tincture of colchicum seed may be given in doses of 30 minims (2.0 mils) every three hours or in amounts sufficient to cause slight looseness of the bowels. The alkaloid, colchicin, is equally effective. It may be given in doses of $\frac{1}{120}$ grain (0.0005 gm.) every four hours until the pain is relieved. The usual dose of cinchophen is about 7 grains (0.5 gm.) every four hours. It is best given in capsules, and should be accompanied

by an alkali, preferably large doses of sodium bicarbonate, to prevent precipitation of the uric acid in the urine before it is passed. Otherwise, alkalies, formerly so much in vogue, have been largely abandoned. Nevertheless, large doses of the organic salts of potassium, especially the citrate, seem to do good. Occasionally, the pain of acute gout is so excruciating that the use of morphin becomes necessary.

The affected member should be elevated, immobilized, and enveloped in cotton wool or hot fomentations (hot saturated solution of magnesium sulphate). Cold applications, leeching, and blistering do not, as a rule, act well.

*Chronic Gout.*—No absolute rule can be laid down regarding the diet. The special features in each case should receive careful study. Some patients do well upon a non-protein diet, others do not. Simplicity and moderation are of the utmost importance. Generally speaking, a diet composed for the most part of milk, farinaceous foods, succulent vegetables, and eggs is most suitable. Owing to the difficulty that gouty patients have in excreting uric acid, it is advisable to exclude from the diet foods which are especially rich in purin bodies, such as sweetbreads, liver, kidneys, peas, beans, and lentils. Concentrated soups, hashes, croquettes, rich pastry, malt liquors, heavy wines and other alcoholic beverages should also be avoided. So far as flesh is concerned, there is no difference between red and white meats, and usually either may be allowed once a day in moderation, unless a coexisting nephritis makes an extreme restriction in the protein intake necessary. Some patients are exceedingly intolerant of acid fruit. Tea and coffee, in moderation, do not appear to be particularly harmful, probably because methylated purins (caffein, theobromin) are in large part destroyed within the body. Water-drinking between meals should be encouraged.

The quantity as well as the character of the food must be regulated. No more should be eaten than is absolutely necessary to satisfy hunger. The patient should be warmly clothed and should avoid as far as possible exposure to sudden atmospheric changes. Systematic exercise in the open air is very beneficial. Well-nourished patients should be urged to take walking trips, to play golf or tennis, or to try horseback riding. When active exercise is not feasible, massage may be strongly recommended. All overwork of mind should be forbidden. Hydrotherapy—tepid sponge-baths and douches—is useful. Heavy robust patients often derive much benefit from the Turkish bath.

Visits to certain mineral springs—Bedford, Saratoga, Harrowgate, Carlsbad, Contrexeville, Aix-les-Bains—are sometimes of value. The good effects of the spa treatment are only in part due to the waters drunk; change of scene, fresh air, strict diet, and freedom from business and household cares are important factors. Residence during the winter months in a dry, warm, inland climate is desirable.

Remedies intended to improve the digestion are frequently indicated. In some cases a combination of an acid and a bitter before meals is of service. Daily action of the bowels should be secured. Of special remedies, those most worthy of consideration are colchicum and arsenic. Colchicum is most effective in the paroxysms, although small doses with alkalies may be of benefit in the intervals. The prolonged use of arsenic occasionally seems to do good. Gudzent, His, Klemperer and others report good results from the ingestion of water impregnated with radium emanation, but Rowntree and Baetjer[1] in a small series of cases were not favorably impressed with the

[1] Jour. Amer. Med. Assoc., Oct. 18, 1913.

treatment, and McCrudden and Sargent[1] were unable to demonstrate any influence from radium therapy on the uric acid content of the blood or on the rate of excretion of uric acid. So-called uric-acid solvents (piperazin, lycetol, quinic acid, etc.) are valueless.

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## DIABETES MELLITUS

**Definition.**—Diabetes mellitus is a chronic disorder of metabolism, involving primarily the carbohydrates, and secondarily also the proteins and fats, and characterized clinically by hyperglycemia, glycosuria, polydypsia, polyuria, emaciation and a pronounced tendency to an acid intoxication resulting in coma.

The term diabetes (*διαβήτης*, a syphon), was first used by Aretæus, a Greek physician of the second century, but the disease itself was undoubtedly known before his time, for it is alluded to in the writings of Celsus (first half of first century A.D.).

**Etiology.**—Diabetes mellitus is a widely distributed disease, but it is *more prevalent in some countries than in others.* Thus Normandy in France, Würtemberg and Thüringen in Germany, Tuscany in Italy, and Ceylon in India are cited as localities in which it is especially common. On the other hand, the Japanese seem to enjoy a relative immunity to diabetes, especially of the severer types. Statistics indicate that the disease is on the increase at least in America and in England. In the registration area of the United States the death-rate from diabetes is at present about double what it was in 1900.

*Race* is not without influence. Hebrews appear to be particularly prone to the disease. In this country the whites suffer relatively more than the blacks. In India the incidence of diabetes among the Hindus is out of all proportion to their numerical strength. All authorities agree that in every community it is the *well-to-do* persons who are most affected by the disease and that *luxurious living* and *sedentary habits* are important factors in its causation. Although diabetes seems sometimes to have its origin in dietetic errors, it is not certain that the excessive use of carbohydrates alone can cause it. The disease cannot be produced in normal animals by prolonged excess of dextrose (Allen[2]); nevertheless in partially depancreatized dogs an excess of carbohydrates soon produces fatal diabetes, whereas a diet of meats keeps the animals free from the disease. An *hereditary* or *familial tendency* to diabetes is clearly shown in from 20 to 25 per cent. of the cases. Von Noorden relates the history of a family in which the disease occurred in 3 generations and J. R. Williams[3] cites two families with diabetes in 4 maternal generations. Langaker[4] refers to a family in which 5 of 8 children died of the disease.

Cases of "*conjugal diabetes*" are not very infrequent. Combining the statistics of a number of writers, Williamson found a total of 56 instances in which both man and wife were affected among 5159 diabetic patients—1.08 per cent. Although some of the cases were suggestive of contagion, similarity of the mode of life seemed amply sufficient to account for most of them.

[1] Amer. Jour. Med. Sci., Nov., 1918.
[2] F. M. Allen: Glycosuria and Diabetes, Boston, 1913.
[3] Amer. Jour. Med. Sci., Sept., 1917.
[4] Deutsch. med. Woch., 1911, xxxvii, 217.

The coexistence of diabetes with *obesity* and with *gout*, especially the former, is a matter of common observation. According to Joslin[1] obesity is coincident with the onset of the disease in 3 cases out of 4.

The association of *acromegaly* and of *hyperthyroidism* with diabetes has been commented upon by a number of writers. In 176 cases of acromegaly collected from the literature, Borchardt[2] found that diabetes was present in 63 and alimentary glycosuria in 8. *Syphilis* does not appear to have much influence on the incidence of diabetes, the Wassermann reactions being positive in only from 5 to 10 per cent. of the cases.

*Injuries* to the head and less frequently to other parts of the body, and *various lesions of the central nervous system*, especially of the brain, not rarely produce glycosuria and sometimes lead to true diabetes. Great anxiety or worry, intense grief, severe fright and other causes of *profound emotional disturbance* or *mental strain* have long been recognized as antecedents of the disease and are believed to be important etiologic factors. Glycosuria is not uncommon in the later weeks of *pregnancy*, and while it is usually transitory, disappearing soon after the birth of the child, it is occasionally the precursor of true diabetes.

Diabetes occurs at all *ages*, but it is most common in middle life, between the ages of 40 and 60. Two and eight-tenths per cent. of von Noorden's[3] 3000 cases and 4.7 per cent. of Joslin's[4] 1156 cases occurred in the first 10 years of life. In 1913, Knox[5] collected 16 cases in the first year of life. As regards *sex*, males are somewhat more frequently affected than females, although apparently more women succumb to the disease than men.

**Morbid Anatomy.**—The body is usually much emaciated and lesions of complicating conditions, such as pneumonia, pulmonary tuberculosis, chronic nephritis, furuncles, carbuncle, localized gangrene, etc., are frequently present. Important changes occur in the *pancreas* and are believed to have etiologic significance. While the changes vary somewhat in character, the most constant are an increase of fibrous tissue between the individual acini and vacuolation, atrophy, and, in places, complete disappearance of the islands of Langerhans (chronic interacinar pancreatitis). Macroscopically, the gland may appear normal, but not infrequently it is small and indurated. Cecil[6] found pancreatic lesions in more than 87 per cent. of 90 cases of diabetes and Weichselbaum[7] in every one of 183 cases. Coarse lesions of the pancreas (carcinomata, cysts, interlobular cirrhosis from obstruction of the ducts, etc.), which only occasionally involve the islands of Langerhans, are not often found at necropsy in diabetes.

The *liver* is commonly enlarged and of a rosy color, and microscopically shows fatty changes and an absence of glycogen granules in the protoplasm of the hepatic cells. Cirrhosis of the liver is sometimes observed, this condition and the chronic pancreatitis probably depending upon the same etiologic factors. Occasionally, the cirrhotic liver and also the pancreas and skin are pigmented (bronzed diabetes, hemochromatosis). In exceptional cases an organic lesion is found at the base of the *brain*. Michael and Osler have each reported a case of diabetes in which a cysticercus occupied the floor of the fourth ventricle and Weichselbaum and Richardiere cases in which there was disseminated sclerosis with sclerotic plaques in the same region.

[1] Med. Clin. of North America, May, 1921.
[2] Zeit. klin. Med., 1908, 66, 332.
[3] Pfaundler u. Schlossmann, Handb. d. Kinderheilk., 1910, ii, 117.
[4] Treatment of Diabetes, 1917, 28.
[5] Johns Hopkins Hosp. Bull., 1913, xxiv., 274.
[6] Jour. of Exper. Med., Mar., 1909.
[7] Wien. klin. Woch., 1911, xxiv, 153.

*General arteriosclerosis* is present in a large proportion of cases. It may be etiologically related to the pancreatic disease and hence to the diabetes, it may possibly be a result of the latter, or it may be merely a concomitant condition.

In a few instances a *large-cell hyperplasia*, resembling that occurring in Gaucher's disease, has been found in the spleen, lymph-nodes and liver (Schultze,[1] Lutz,[2] Williams and Dresbach.[3]) It seems to have some relation to the lipoidemia that is observed clinically, but its actual significance is not known.

**Pathogenesis.**—Various theories have been advanced from time to time to account for the essential feature of diabetes mellitus, namely the hyperglycemia, or excess of sugar in the blood, but the ultimate nature of the process is still obscure. Undoubtedly the *pancreas* is the organ that is chiefly concerned in producing the disease. Extirpation of the pancreas in animals, as von Mering and Minkowski first pointed out, is invariably followed by hyperglycemia, glycosuria and all the phenomena of true diabetes, and numerous observations have shown that this organ is the site of pathologic changes in the large majority of cases of diabetes in man. Acute fulminating pancreatitis with complete destruction of the pancrease does not usually produce glycosuria because of the inhibitory action of the profound intoxication and the rapidity with which death ensues. That the influence of the pancreas on carbohydrate metabolism is independent of its digestive functions is also clearly proved by the results of ligature of the duct of Wirsung, and that it depends upon an internal secretion, while not proved, is almost certain. Whether this hypothetic secretion is the product of the special groups of cells known as the islands of Langerhans is not definitely known, yet the studies of Opie,[4] of Wright and Joslin,[5] of Weichselbaum and Stangl,[6] and of others indicate that such is the case. Apparently, the loss of the pancreas prevents the hepatic cells from forming and storing glycogen or leads to excessive glycogenolysis with an overproduction of sugar, but more important still, it seems to destroy the power of the tissues to utilize sugar, either by producing an alteration in the sugar itself or by affecting some change in the tissues. Allen believes that normally sugar exists in the blood only in colloid combination and that the combining substance, which he likens to an amboceptor, is supplied by the pancreas. It is likely that the disease of the pancreas manifesting itself as diabetes, is at first sometimes functional, otherwise it would be difficult to explain the greatly increased tolerance for carbohydrates that diabetics not rarely acquire through fasting.

The important parts played by the *liver* in carbohydrate metabolism (glycogenesis, glycogenolysis and glyconeogenesis[7]) naturally led to the conclusion that hepatic disease was the essential factor in the genesis of diabetes. To-day, however, this view has few adherents. Lesions of the liver are not at all constant in diabetes and when present are usually correlated with definite changes in the pancreas, and, on the other hand, glycosuria, even the alimentary form, is rarely found among the symptoms of hepatic insufficiency in such diseases as acute yellow atrophy, cirrhosis, etc. It is improbable, therefore, that a morbid condition localized solely in the liver can

[1] Verhandl. d. deutsch. path. Gesellsch., Strassburg, 15 Tag., 1912.
[2] Ziegler's Beiträge, 1914, lviii, 273.
[3] Amer. Jour. Med. Sci., Jan., 1917.
[4] Diseases of the Pancreas, 1903.
[5] Jour. Med. Research, 1902, i, No. 2.
[6] Wien klin. Woch., Sept. 18, 1902.
[7] The formation of glycogen from compounds other than sugars and starches, such as protein and possibly fat.

originate true diabetes. Nevertheless, the liver is not without influence, although the rôle that it plays is probably a passive one

The liver in diabetes loses its power to form glycogen from the sugars brought to it or to store this substance after it has already been formed, and moreover in frogs depancreatization does not cause glycosuria if the liver has been previously removed. It is possible, too, that the liver may activate the pancreatic secretion, for Hedon has shown that pancreatic extract when injected into the portal vein of depancreatized dogs greatly lessens the glycosuria, but is without effect when injected into the general circulation.

It is generally conceded that carbohydrate control is to some extent under the influence of the *nervous system*. This influence is shown in the glycosuria resulting from Bernard's classical piqûre in the floor of the fourth ventricle and from other experimental or accidental injuries to the brain, and again in the recorded instances in which true diabetes has been occasioned by tumor or other lesions of the pons, medulla or cerebellum. The experimental evidence indicates that glycosuria after piqûre depends upon the excessive mobilization of sugar by the liver and is effected by stimulation of the sympathetics, not directly, however, but through the intervention of the adrenals, for the glycosuria does not occur if the liver is rendered glycogen free, if the sympathetics are divided, or if the adrenals are removed, or even if the left splanchnic, which supplies both adrenals, is divided. It is Allen's conception, that nervous disorder is primary in diabetes and that the changes in the islands of Langerhans are secondary.

Besides the pancreas, *other glands of internal secretion* undoubtedly play some part in carbohydrate metabolism, but the exact manner in which they operate remains obscure. Injections of epinephrin and stimulation of the adrenals cause glycosuria in dogs, even when these animals have been fasted, and increase the glycosuria occurring in diabetes; further, as already stated, Bernard's piqûre is without effect after removal of the adrenals. It is likely that the function of adrenals is opposed to that of the pancreas and that epinephrin favors the mobilization of sugar by stimulating the sympathetic endings in the liver, for its action is offset by ergotoxin and other agents that paralyze the sympathetic endings.

The hypophysis seems to have an influence on carbohydrate metabolism similar to that of the adrenals and to operate through the sympathetic system; indeed, Cushing believes that the glycosuria resulting from Bernard's piqûre is an hypophyseal effect, for the site of the puncture is close to the hypophysis. Puncture of the hypophysis itself induces glycosuria, and after hypophysectomy stimulation of the sympathetics no longer causes glycosuria.

The influence of the thyroid upon carbohydrate metabolism is no less important than that of the adrenals. Hyperthyroidism is usually associated with lowered carbohydrate tolerance, and neither Bernard's piqûre nor injection of adrenalin produces glycosuria after thyroidectomy. Apparently, the thyroid inhibits the function of the pancreas and augments that of the adrenals. While it is evident from the foregoing that disturbances of carbohydrate metabolism may have their source in various derangements of endocrine equilibrium, it must be borne in mind that *the essential feature in diabetes is an inability to utilize sugar rather than overproduction of sugar and that thus far the disease has never been reproduced experimentally in any way other than by removal of the pancreas.*

In true diabetes, as contrasted with simple glycosuria, the capacity of the tissues to "burn" sugar is always more or less impaired. When carbohydrates cannot be utilized and even when carbohydrates are not available for oxidation, as in complete starvation, there occurs, for some unknown reason,

an incomplete combustion of fat, intermediate products of fat catabolism appearing in the blood and urine. These intermediate products comprise the so-called ketone bodies—acetone, diacetic acid and β-oxybutyric acid—which normally are reduced to carbon dioxid and water. Their presence in diabetes depends upon excessive production and failure of oxidation. While ketones are derived chiefly from fat, a small proportion may come also from protein, for amino-acids that fail to yield sugar (leucin and tyrosin) are readily transformed into diacetic and β-oxybutyric acids. For a time the urine may contain only acetone and diacetic acid, but eventually in severe cases β-oxybutyric acid also appears. Acetone itself in the quantity present is not harmful, but the acids act injuriously by abstracting bases from the tissues, thus producing a condition known as *acidosis* (see p. 386). It is possible that β-oxybutyric acid acts also as a specific poison. The *intense dyspnea* or air hunger occurring in acidosis probably depends upon an accumulation of carbon dioxid in the cells, the blood being unable to abstract it owing to a deficiency of available alkali.

The profound disturbance of fat metabolism may also be indicated by an accumulation of a large amount of fat in the blood (*lipemia*), the latter in consequence becoming turbid. The fat is apparently derived chiefly from the food (Bloor), but it is possible that a part may come from the tissues (Epstein, Klemperer, Fischer). Diabetic lipemia is always accompanied by acidosis, although the latter frequently occurs without lipemia.

The *glycosuria* occurring in diabetes mellitus and indeed all other glycosurias, save that resulting from the administration of phloridzin and that due to so-called renal diabetes (see p. 370), depend upon hyperglycemia, sugar always appearing in the urine when the blood-sugar concentration exceeds the threshold of renal permeability. In diabetes the blood-sugar may be derived not only from the carbohydrates of the food, but also in severe cases from protein, and possibly from fat. All portions of the protein molecule do not yield sugar and some proteins supply more sugar than others. In severe diabetes when carbohydrates are no longer available, the amount of sugar excreted bears a constant relation to amount of nitrogen excreted. This dextrose-nitrogen (D:N) ratio in some cases being as high as 3.65 to 1.

The *asthenia*, which is a conspicuous symptom in many cases of diabetes is probably due chiefly to the glycosuria, the daily loss of sugar from an inability of the tissues to utilize it sometimes equalling the average caloric requirements of a healthy person. Other factors, however, may be a loss of body fat, impaired digestion, and, according to Allen,[1] the specific endocrine deficiency.

The *polyuria* of diabetes is a result of the diuretic action of the blood-sugar, which Allen assumes acts as a crystalloid and not as if it were in colloid combination. The *polydipsia* is, of course, also dependent upon the hyperglycemia. According to Luckhardt,[2] the *voracious appetite* occurring in many cases of diabetes is to be ascribed not so much to undernutrition as to an increase in the intensity of the contractions (hunger contractions) of the empty stomach resulting from the pancreatic insufficiency.

**Symptoms.**—Diabetes usually begins insidiously and pursues a chronic, course. There are cases, however, in which the onset is sudden, and others, especially in children and young adults, in which the progress is exceedingly rapid. The most prominent symptoms are the excretion of an abnormally large amount of urine containing glucose, frequent micturition, excessive thirst, asthenia and emaciation; but in addition to these there are many

[1] Amer. Jour. Med. Sci., Mar., 1921.
[2] Amer. Jour. of Physiol., 1914, xxxiii, 313.

others, any one of which in individual cases may be a conspicuous feature or at least the first to attract attention.

*The Urine.*—The quantity of urine varies considerably, although as a rule it is much increased, from 3 to 9 liters (100–300 ounces) a day being a common amount. Sometimes, especially when little water is drunk or there is diarrhea, the quantity of urine exceeds but little, if at all, the normal (*diabetes decipiens*). The urine is usually pale and clear and in severe cases may have a peculiar odor resembling that of ripe fruit or new hay, owing to the presence of acetone. Notwithstanding the large quantity that is voided, the specific gravity is, as a rule, abnormally high, 1025 to 1050, but occasionally, even with marked glycosuria, it is normal or below normal. The reaction is almost always acid. The amount of glucose excreted varies in different cases and at different times in the same case, being markedly influenced by the diet and the permeability of the kidneys. Mere traces may be present, but ordinarily the percentage ranges between 1 and 10 per cent., and the daily output between 30 grams (1 ounce) and 800 grams (25 ounces). These figures, however, may be considerably higher. The glycosuria is increased after meals, especially if they include much starchy or saccharine food, and is decreased after fasting. In mild cases urine passed in the early morning may be free from sugar. In severe cases more sugar is excreted than corrsponds to the amount of carbohydrate ingested, the excess being derived from protein and possibly from fat. Usually the percentage of sugar in the urine and the concentration of sugar in the blood are roughly parallel, but there are many exceptions to this rule. Somewhat frequently there is little or no glycosuria when the hyperglycemia is marked and occasionally there is pronounced glycosuria when the percentage of blood-sugar is below the normal level. Nephritis usually, but not invariably, decreases the permeability of the kidneys for glucose and not rarely even in the absence of nephritis the threshold of renal retention is abnormally high. With the coming of diabetic coma and during intercurrent infections, glycosuria may entirely disappear, while the blood-sugar concentration rises.

In severe diabetes, when the fats are attacked, acetone or ketone bodies commonly appear in the urine. Acetone appears first, then diacetic acid, and finally $\beta$-oxybutyric acid, the daily output of the last sometimes reaches 50 to 80 grams. A large amount of the ketone acids is usually accompanied by pronounced glycosuria, but there is by no means always a constant relation, and, therefore, even in apparently mild cases of diabetes the urine should be tested at frequent intervals with ferric chlorid, a positive reaction being significant of approaching danger. Coincident with the appearance of the ketone acids in the urine there is an excessive excretion of ammonia, this substance, which is produced by the decomposition of protein, being diverted from urea formation to neutralize the abnormal acidity and afterward eliminated by the kidneys. The amount of ammonia in the urine may be increased from the normal of 0.5 to 1.5 grams daily to from 3 to 8 grams or more, and instead of forming from 2 to 5 per cent. of the total nitrogen, it may form 10 to 20 per cent. In a case cited by Jonas and Pepper[1] the daily elimination of ammonia exceeded 31 grams.

Albuminuria occurs at some time in more than one-third of the cases. It may be due (*a*) to slight irritation of the kidneys by the saccharine urine, (*b*) to concomitant nephritis, or (*c*) to irritation of the kidneys by acid bodies. This last is seen in grave cases on the approach of coma and is usually accompanied by "showers" of hyaline or finely granular casts (Külz's sign of impending coma).

[1] Jour. Amer. Med. Assoc., June 23, 1917.

Intolerable itching at the end of the urethra in males or of the vulva in females, due to the irritant action of the saccharine urine on these parts, is sometimes the first symptom to direct attention to the disease. Less frequently balanitis or vulvitis results from the same cause.

*The Blood.*—The characteristic blood change is the hyperglycemia. The concentration of sugar in the blood of normal persons varies between 0.06 per cent. and 0.12 per cent., the average being about 0.08 per cent. The concentration increases after meals, reaching its height in from 1 to 2 hours, and then gradually decreases. In diabetes the sugar content of the blood is definitely increased, the concentration ranging from 0.14 per cent. to 0.5 per cent.

As a result of the partial failure of fat catabolism the blood of diabetics often contains an excess of fat (lipemia). In severe cases it may have a turbid or even a milky appearance and show under the microscope numerous highly refractive droplets, which stain black with osmic acid. In many cases, however, the fat, though excessive, is invisible being in the form of lipoids (lecithin, cholesterol). In general the amount of fatty matter in the blood (lipins[1]) increases with the severity of the disease, the amount ranging from the normal (0.59 per cent.) to 0.8 per cent. in mild cases and to 1.4 per cent. in severe cases. With the occurrence of acidosis there is a decrease in the reserve alkali of the body and this is shown in a reduction of the blood $CO_2$ content from the normal of 60 to 70 volumes per cent. to 30 or even 20 per cent.

Except in advanced cases, when there may be a moderate anemia, the erythrocyte count is about normal, although occasionally, probably owing to a temporary concentration of the blood, it may be somewhat high. In the absence of complications there is no numerical change in the leucocytes.

*The Digestive Tract.*—One of the earliest and most distressing symptoms resulting from the hyperglycemia is the excessive thirst, the amount of water consumed being roughly parallel to the intensity of the polyuria. The appetite, also, is often inordinate. The mouth and tongue are usually dry, sticky, and abnormally red. The gums show a tendency to shrink and the teeth to loosen and decay. Despite the intake of enormous amounts of fluid, the digestion in the early stages of the disease is, as a rule, remarkably good. In the later stages, high gastric acidity with postprandial discomfort sometimes occurs and upon the approach of coma pronounced gastro-intestinal disturbances are common. Constipation is the rule, but from time to time, as a result of an unsuitable diet or of concomitant catarrh of the bowel, there may be diarrhea.

*The General Nutrition.*—As the disease progresses muscular weakness and emaciation almost invariably supervene, in some cases rapidly (*diabète maigre*) and in other cases slowly, the patient sometimes remaining fairly vigorous and well nourished, or even corpulent, if he were so when first stricken, for many years (diabète gras). The skin is often harsh and dry and the hair lusterless. The nails, too, may be abnormally brittle. In many of the more severe cases the temperature is slightly below normal. As a result of undernutrition the basal metabolism may be considerably decreased. In the later stages, especially during fasting, general edema is not uncommon even when there is no evidence of renal or cardiac disease. It may be due to excessive salt intake or, as Wilder and Beeler[2] have suggested, to extreme inanition. It sometimes masks the emaciation.

[1] The term *lipins* has been proposed for the entire group of ether-soluble constituents, including the ordinary fats and the lipoids, the chief of which are lecithin and cholesterol.

[2] Amer. Jour. of Physiol., 1921, 55, 287.

*The Nervous System.*—Loss of sexual power, usually permanent, is a common symptom. Diminution or loss of the knee-jerks is frequently observed, and is probably a result of peripheral neuritis. Cases presenting many of the symptoms of tabes (diabetic neurotabes) have been described. Various forms of paresthesia, cramps in the muscles of the legs, and neuralgic attacks are also of frequent occurrence. Bilateral sciatica is sometimes observed, but is less common than several writers have stated. Mentally, the patient is often inclined to be depressed and irritable, although his intellectual capacity is rarely impaired.

According to the degree with which appropriate dietetic treatment is carried out, diabetic coma eventually ensues in from one-half to three-fourths of all cases. It may develop without obvious cause or it may be precipitated by excessive physical or mental strain, nervous shock, traumatic injury, intercurrent disease, or dietetic indiscretions. In many cases its approach is foreshadowed by extreme languor and restlessness, by pronounced gastrointestinal disturbances, such as epigastric pain, nausea, vomiting and diarrhea, by the sudden disappearance of sugar from the urine, or by the occurrence of albuminuria with "showers" of tube-casts. Of more certain value, however, than any of these signs are the color reaction in the urine with an aqueous solution of ferric chlorid and the various other laboratory findings indicative of acidosis (see p. 386).

In the usual type of diabetic coma (Kussmaul type[1]), the chief features are drowsiness, gradually deepening into coma, subnormal temperature, a frequent small pulse, and a characteristic form of dyspnea (air-hunger), in which the respirations are remarkably deep and long, but not necessarily accelerated. Cyanosis is absent, at least at the beginning, and convulsions are comparatively rare, although either generalized epileptiform seizures or Jacksonian attacks may occur. A peculiar sweetish or fruity odor to the breath is sometimes observed. Diminished tension of the eye-ball has not rarely been observed (Krause, Heine, Schütz, Riesman[2]). Exceptionally the reaction for diacetic acid in the urine disappears during the coma. Death usually ensues in from a few hours to several days. Partial recovery and even a complete subsidence of the symptoms may occur, but is rare. Occasionally, dyspnea is absent and the only symptoms accompanying the coma are those of collapse, and still more rarely the symptoms resemble those of alcoholic intoxication, but consciousness is never regained and death occurs within a few hours.

*Diabetes in Childhood.*—The symptoms of diabetes in young children do not differ materially from those in adults. The conspicuous features are excessive thrist, irritability, emaciation, and nocturnal incontinence of urine from polyuria. Gangrene is rare. The course is usually very rapid and death in coma is the rule. Külz[3] found that of 46 diabetic children more than 50 per cent died within 3 months. Occasionally, the duration appears to be only two or three weeks. In rare instances, however, the disease is of a mild type and the symptoms remain stationary or even subside under appropriate treatment.

*Hemochromatosis with Diabetes* (*Diabète Bronzé*).—The bronzed diabetes of Hanot and Chauffard[4] and other French writers is now recognized as being a terminal stage of hemochromatosis—a rare condition, first described by von Recklinghausen,[5] in 1889, in which there is pigmentation of the

[1] Deutsch. Archiv. f. klin. Med., 1874, iv.
[2] Jour. Amer. Med. Assoc., Jan. 8, 1916
[3] Gerhardt's Handbuch d. Kinder., 1878, vol. iii.
[4] Rev. de Méd., 1882.
[5] Tageblatt der Natur. zu Heidelberg, 1889.

viscera and usually also of the skin, with interstitial fibrosis of the liver and pancreas. When the cirrhosis of the pancreas reaches such a degree that the islands of Langerhans are involved diabetes supervenes. It is probable, but not proved, that both the pigmentation, which depends upon a deposition of hemosiderin and hemofuscin in the tissues, and the fibrotic changes in the liver and pancreas are the result of some obscure intoxication. There is no evidence of excessive hemolysis and apparently the deposit of iron and other pigment is caused by interference with excretion (Meltzer and Parker, Gaskell and Sladden[1]).

According to Sprunt,[2] 63 cases of hemochromatosis had been reported up to 1911, and of these 50 were accompanied by diabetes. In only two or three instances has the disease occurred in females. Clinically, the picture is one of rapidly fatal diabetes with cirrhosis of the liver. Bronzing of the skin is present in the large majority of cases, but is not constant. In only 1 of 30 cases analyzed by Blumer,[3] did the patient live more than 2 years after the onset of the diabetes.

**Complications.**—*Pulmonary tuberculosis* occurs somewhat frequently, especially among patients of the poorer classes, and may be the immediate cause of death. Apparently, however, it is much less common than formerly. Older statisticians reported an incidence as high as 40 or even 50 per cent. As a rule, the disease develops insidiously and pursues a somewhat rapid course. During its progress the glycosuria, but not the hyperglycemia, may diminish or actually disappear. *Pneumonia* is also comparatively common, especially in the later stages of the disease. It is an exceedingly dangerous complication and even when not productive of fatal coma not rarely results in *abscess* or *gangrene of the lung*. Cutaneous affections of various kinds are very prone to develop. One of the earliest to appear is *pruritus of the external genitals*. In many cases the itching is followed by a refractory form of *eczema*. Less frequently, there is *generalized pruritus*.

*Boils* and *carbuncles* very often occur and are to be ascribed to diminished resistance to bacterial infection. The peculiar dermatosis known as *xanthoma diabeticorum* is occasionally observed. It occurs upon the trunk and limbs as pea-sized yellowish or yellowish-red papules, firm to the touch and slightly tender. The lesions develop rapidly and usually disappear with improvement in the diabetes. A number of cases of *perforating ulcer of the foot* are on record (Sample and Gorham[4]). *Gangrene* in various parts of the body, especially in the extremities, occurs with considerable frequency. It is observed chiefly in the old and more often in men than in women. It may be of the moist variety and supervene upon a slight wound or contusion, but as a rule, it is dry and develops spontaneously in consequence of *sclerosis of the peripheral arteries*, which is a frequent concomitant of diabetes. *Gingivitis* with *pyorrhea alveolaris* often occurs.

*Peripheral neuritis* is by no means uncommon. In mild cases absence of the knee-jerk may be the only indication. In other cases there is severe neuralgia, affecting especially the trifacial and sciatic nerves. Numbness, tingling, and other forms of paresthesia may also occur. Occasionally, motor paralysis involving groups of muscles or whole limbs is a conspicuous feature of the neuritis. Several writers have described cases of *pseudo-tabes* with lancinating pains, areas of anesthesia, loss of the deep reflexes, and ataxia, but without the Argyll-Robertson pupil or disturbance of the sphincters.

[1] Quart. Jour. Med., Jan., 1914.
[2] Arch. Int. Med., 1911, viii, 75.
[3] New York Med. Jour., Nov. 4, 1911.
[4] Johns Hopkins Hosp. Bull., Jan., 1913.

*Cataract*, usually of the soft variety and bilateral, occurs in about 5 per cent. of the cases. Other ocular changes are also observed. They vary in severity from *slight failure of accommodation* to *extensive hemorrhagic retinitis* and *total optic-nerve atrophy*. *Otitis media* occasionally develops suddenly.

Of the complications affecting the genito-urinary tract, mention has already been made of *chronic nephritis*, *inflammation of the external genitals*, and *loss of sexual power*. In addition to these, *cystitis* from bacterial invasion of the urine, is occasionally seen. *Pneumaturia* from the same cause has also been reported. *Amenorrhea* is not uncommon. *Pregnancy* may occur in diabetes, especially in the early stages, but each condition has a maleficent influence on the other. Offergeld[1] states that of 57 diabetic women 50 per cent. died during or soon after childbirth and of the children, 51 per cent. were stillborn and 11 per cent. died soon after birth. However, under modern methods of treatment the prognosis is more favorable.

**Diagnosis.**—In testing the urine for sugar, a portion of a twenty-four hour collection or, preferably, a specimen that has been passed two or three hours after the heaviest meal of the day should always be chosen. Care must be taken also not to mistake other copper-reducing substances for dextrose. The exclusion of *uric acid*, *creatinin* and *indican*, which in excess reduce copper solutions, is usually not difficult. *Glycuronic acid salts* are occasionally observed independently of glycosuria after the ingestion of certain drugs. These are capable of reducing copper solution, but not of fermenting. *Milk sugar*, which is not rarely found in the urine of nursing women, resembles dextrose in its reactions, but it does not ferment within 18 hours. *Maltose* and *levulose* reduce alkaline copper solutions and also respond to the fermentation test, but they are nearly always found in association with dextrose. *Pentoses* are also an occasional source of error. They reduce Fehling's solution after prolonged heating and respond to the phenylhydrazin test, but do not ferment and are optically inactive. *Alkapton* reacts positively with copper solutions, but urine containing it turns black on standing or on the addition of an alkali and does not ferment with yeast. Finally, the possibility of *malingering* must be borne in mind, as sugar may be introduced into the urine for the purpose of deceiving.

The importance of determining the concentration of sugar in the blood, as well as of testing the urine, in suspicious cases is shown by the fact that normal persons occasionally have a low renal threshold and sugar appears in the urine even when there is no hyperglycemia (renal diabetes), and, on the other hand, that in true diabetes the renal permeability is sometimes much decreased and little or no sugar appears in the urine, although the blood-sugar level is very high. The essentials for the diagnosis of *renal diabetes* are a low or normal blood-sugar content, persistent glycosuria which is not influenced by an increase or decrease of the intake of carbohydrate, and an absence of the usual symptoms of ordinary diabetes mellitus.

It is doubtful whether any sharp distinction can be drawn between *alimentary glycosuria* and diabetes. While it is true that in severe diabetes the glycosuria persists to a greater or less extent in the absence of all carbohydrate food, and even for a time during fasting, it is well recognized that in all grades of the disease the glycosuria is in large part alimentary and that in mild cases it is possible to prevent the appearance of sugar in the urine by reducing the intake of carbohydrate. It is advisable, therefore, to regard any person who after taking 100 grams of glucose on an empty stomach has glycosuria and a blood-sugar concentration above 0.15 per cent. as a potential, if not an actual, diabetic.

[1] Deutsch. med. Woch., 1909, xxxv, 28.

**Prognosis.**—Diabetes varies considerably in its course and duration. It may be extremely malignant and terminate fatally within a few weeks or it may be very mild and last for 15 or 20 years, or longer, even with sugar persistently appearing in the urine. The chief factors to be considered in determining the prognosis in individual cases are the age of the patient, the family history, the daily output of sugar in the urine or, preferably, the degree of hyperglycemia, the presence or absence of ketonuria, the duration of the disease, the degree of tolerance for carbohydrate, the general condition of the patient, the presence or absence of complications, such as tuberculosis and nephritis, and the willingness and ability of the patient to carry out appropriate treatment. After the first three decades, in which the disease is, as a rule, of the shortest duration, age is a factor of secondary importance. Except in children, an hereditary tendency is unfavorable rather than favorable to long life. The more pronounced the glycosuria and the greater the intolerance to carbohydrate, the more serious is the outlook. Diabetes is usually considered to be severe when the patient continues to excrete sugar while on an exclusive protein-fat diet or is receiving at most 10 grams of carbohydrate a day in the form of green vegetables. In mild cases 30 grams or more of carbohydrate may be taken in the twenty-four hours without causing glycosuria.

While the tendency to acidosis is usually greater in proportion to the degree of glycosuria, this is by no means always the case. Mild cases of diabetes may show pronounced acidosis, and severe cases may show no acidosis. It must be borne in mind, also, that mild cases frequently become severe through neglect of treatment. The earlier the patient is put upon an appropriate regimen the better, in general, is the outlook. The most favorable cases, as a rule, are those of not more than moderate severity, occurring in middle-aged persons, who are more or less obese, and who are willing and sufficiently intelligent to carry out the required treatment. Even a considerable degree of ketonuria in such cases is not incompatible with long life, if there is no nephritis or cardio-vascular disease. Unfortunately in diabetes, as in syphilis, control of the patient is frequently lost as soon as the obtrusive symptoms have disappeared. Actual cure, in the sense of a complete restoration of carbohydrate tolerance, is rarely attained.

The chief causes of death in diabetes are coma (about two-thirds of the cases), cardiovascular accidents (cardiac insufficiency, angina pectoris, cerebral hemorrhage, gangrene), pneumonia, tuberculosis and carbuncle. While coma is by far the commonest cause of death, it must not be forgotten that it is often precipitated by some other condition, such as intercurrent infection and cardiac or renal insufficiency.

**Treatment.**—As we have no means at present of directly increasing the hypothetic secretion of the pancreas, our efforts must be directed to relieving the strain on the overtaxed gland and rendering its function more effective by restricting the carbohydrate of the diet or, if necessary, restricting the total diet, thus reducing the volume of tissue to be served by the gland. In mild cases of diabetes the restriction of sugars and starches, and to a less extent of fat and protein, so that the entire food intake is well within the assimilative capacity of the patient, is usually sufficient to remove both the glycosuria and the hyperglycemia.

Frequently in the milder cases a carbohydrate-free diet of 1500 to 1600 calories will soon render the patient aglycosuric, and after this has been accomplished and maintained for a few days it will be found possible to order starches in gradually increasing amounts. As a rule, however, it is advisable to maintain the carbohydrate level at 25 per cent. below that of the patient's

maximum tolerance, to keep the fat within 200 grams and the total diet within 2200 calories, and to introduce at intervals of a week or ten days a fast-day, or a day in which the diet is restricted to 5 per cent. vegetables and one-half the usual quantity of fat and protein. The urine should be examined at frequent intervals—at first once or twice a week—and should glycosuria reappear, it should be checked by a return to the original carbohydrate-free diet or a fast day. The following table, which is that compiled by Joslin, with slight modifications, indicates the carbohydrate, fat and protein content of important foods and their caloric value.

DIET TABLE.

Strict Diet: meats (except liver), fish (except roe), broths, eggs, butter, olive oil, coffee and tea, cheese, pepper, salt mustard, vinegar.

Water, clear broths, coffee, tea, cocoa shells can be taken without allowance for food content.

FOODS ARRANGED APPROXIMATELY ACCORDING TO CONTENT OF CARBOHYDRATES

| | 5 per cent.* | 10 per cent. * | 15 per cent. | 20 per cent. |
|---|---|---|---|---|
| VEGETABLES (fresh or canned) | Lettuce<br>Cucumbers<br>Spinach<br>Asparagus<br>Rhubarb<br>Endive<br>Marrow<br>Sorrel<br>Sauerkraut<br>Beet greens<br>Dandelion greens<br>Swiss chard<br>Celery<br>Mushrooms<br>Tomatoes<br>Brussels sprouts<br>Water cress<br>Sea kale<br>Okra<br>Cauliflower<br>Egg plant<br>Cabbage<br>Radishes<br>Leeks<br>String beans canned<br>Broccoli<br>Artichokes canned | String beans<br>Pumpkin<br>Turnip<br>Kohl-rabi<br>Squash<br>Beets<br>Carrots<br>Onions<br>Green peas canned | Green peas<br>Artichokes<br>Parsnips<br>Canned lima beans | Potatoes<br>Shell beans<br>Baked beans<br>Green corn<br>Boiled rice<br>Boiled macaroni |
| FRUITS | Ripe olives (20 per cent. fat)<br>Grape fruit | Watermelon<br>Strawberries<br>Lemons<br>Cranberries<br>Peaches<br>Pineapple<br>Blackberries<br>Gooseberries<br>Oranges | Raspberries<br>Currants<br>Apricots<br>Pears<br>Apples<br>Huckleberries<br>Blueberries<br>Cherries | Plums<br>Bananas<br>Prunes |
| Nuts | Butternuts<br>Pignolias | Brazil nuts<br>Black walnuts<br>Hickory<br>Pecans<br>Filberts | Almonds<br>Walnuts (Eng.)<br>Beechnuts<br>Pistachios<br>Pine nuts | Peanuts<br>40 per cent.<br>Chestnuts |
| Misc. | Clams<br>Scallops<br>Oysters<br>Liver<br>Fish roe | | | |

* Reckon *actual available* carbohydrates in vegetables of 5 per cent. group as 3 per cent., of 10 per cent. group as 6 per cent.

| (30 grams 1 oz.) Contain approximately | Carbohydrates, grams | Protein, grams | Fat, grams | Calories |
|---|---|---|---|---|
| Oatmeal, dry weight | 20 | 5 | 2 | 120 |
| Shredded Wheat | 23 | 3 | 0 | 104 |
| Cream, 40 per cent | 1 | 1 | 12 | 120 |
| Cream, 20 per cent | 1 | 1 | 6 | 60 |
| Milk | 1.5 | 1 | 1 | 20 |
| Brazil nuts | 2 | 5 | 20 | 210 |
| Oysters, six | 4 | 6 | 1 | 50 |
| Meat (uncooked, lean) | 0 | 6 | 3 | 50 |
| Meat (cooked, lean) | 0 | 8 | 5 | 75 |
| Bacon (cooked) | 0 | 5 | 15 | 155 |
| Cheese | 0 | 8 | 11 | 135 |
| Egg (one) | 0 | 6 | 6 | 75 |
| Vegetables, 5 per cent. group | 1 | 0.5 | 0 | 6 |
| Vegetables, 10 per cent. group | 2 | 0.5 | 0 | 10 |
| Potato | 6 | 1 | 0 | 30 |
| Bread | 18 | 3 | 0 | 90 |
| Butter | 0 | 0 | 25 | 225 |
| Oil | 0 | 0 | 30 | 270 |
| Fish, cod, haddock (cooked) | 0 | 6 | 0 | 25 |
| Broth | 0 | 0.7 | 0 | 3 |
| Fruit, 10 per cent | 3 | 0 | 0 | 12 |

1 gm. protein, 4 calories.
1 gm. fat, 9 calories.
1 gm. carbohydrate, 4 calories.
30 gm. alcohol, 7 calories.
30 gm. alcohol, 7 calories.
30 gm. = 1 ounce.
1 kilogram = 2.2 pounds.

A patient "at rest" requires from 25 to 30 calories per kilogram body weight. Growing children may require 50 calories or more per kilogram.

In severe cases the urine cannot be rendered sugar free by a partial reduction of the diet and recourse must be had to a more drastic method of treatment, such as that of prolonged fasting, originally suggested by Guelpa[1] and later elaborated and put on a rational basis by Allen.[2] The points emphasized by Allen are the importance of quickly relieving the pancreatic strain by prolonged fasting, the insidiously harmful effect of a long-continued diet rich in fat, and the necessity of maintaining pancreatic rest even at the expense of the body weight. Joslin[3] gives the following excellent summary of the fasting treatment.

**Preparations for Fasting.**—In severe, long-standing cases, obese and elderly cases, as well as in all cases with acidosis, or in any case if desired, without otherwise changing habits or diet, omit fat, after two days decrease protein and halve the carbohydrates daily until the patient is taking 30 grams or less; then fast. In other cases begin fasting at once.

**Fasting.**—Fast four days, unless earlier sugar-free. Allow water freely, tea, coffee, and thin clear meat broths as desired.

**Intermittent Fasting.**—If glycosuria persists at the end of four days, give 1 gram protein or 0.5 gram carbohydrate per kilogram body weight for two days and then fast again for three days, unless earlier sugar-free. If glycosuria remains repeat, and then fast for one or two days as necessary. If there is still sugar, give protein as before for four days and then fast one, and then gradually increase the periods of feeding, one day each time, until fasting one day each week.

[1] Guelpa (Paris); Autointoxication and Disintoxication, London, 1912.
[2] Boston Med. and Surg. Jour., Feb. 18, 1915; Amer. Jour. Med. Sci., Oct., 1915; Jour. Amer. Med. Assoc., Feb. 28, 1920.
[3] Joslin, E. P.: The Treatment of Diabetes Mellitus, Phila., 1916.

**Carbohydrate Tolerance.**—When the twenty-four hour-urine is free from sugar give 5 or 10 grams carbohydrate (150 to 300 grams of 5 per cent. vegetables) and continue to add 5 or 10 grams carbohydrate daily (more in mild cases) up to 50 grams or more until sugar appears, then fast until sugar-free.

**Protein Tolerance.**—When the urine is again sugar-free decrease the carbohydrate by one-third below the carbohydrate tolerance or at least 10 grams, and then add about 20 grams protein and thereafter 15 grams daily in the form of egg-white, fish or lean meat (chicken) until the patient is receiving from 1 gram to 1.5 grams protein per kilogram body-weight.

**Fat Tolerance.**—It is usually desirable, especially in the young, to add no fat until the protein reaches 1 gram to 1.5 grams per kilogram body weight and the blood sugar is normal. Then 5 to 25 grams daily according to previous acidosis until the patient ceases to lose weight or receives in the total diet 20 to 30 calories per kilogram body weight.

**Reappearance of Sugar.**—The return of sugar demands fasting for twenty-four hours, or until sugar-free. Resume the former diet adding fat gradually and last of all in order to maintain as high a carbohydrate tolerance as possible, sacrificing body weight for this purpose.

**Weekly Fast Days.**—Whenever the tolerance is less than 20 grams carbohydrate, fasting should be practised one day in seven; when the tolerance is over 20 grams of carbohydrate cut the diet in half on one day each week.

The foods commonly employed in determining the tolerance for carbohydrate and protein are 5 per cent. vegetables, oranges, grape-fruit, oatmeal or shredded wheat, potato, fish, chicken, lean meat, skimmed milk.

During the fasting period weak patients should remain in bed. For vigorous patients exercise is indicated, as it seems to increase carbohydrate tolerance. Pronounced fatigue, however, must always be avoided. Alcohol, to the extent of 3 or 4 ounces (90–120 mils) of whisky or brandy a day, may be given during the fast, although it is not usually necessary. Water may be allowed in any amount and tea, black coffee, and clear broth in moderation. In some cases modifications of the treatment are necessary. If the patient is unable to utilize the small amount of carbohydrate contained in the green vegetables, these may be boiled in three changes of water, and the latter discarded. Tuberculosis is not in itself a contraindication to fasting treatment, as the removal of glycosuria and acidosis is of primary importance; nevertheless in some instances the results are not good. Occasionally treatment by undernutrition requires modification because hypoglycemia (below 0.06 per cent.), which is of ill omen, supervenes (Joslin).

A stay of two or three weeks in an institution at the onset is very desirable, for during this period the patient can be taught how to readjust his life and made to understand the necessity of being under supervision. If sufficiently intelligent, he can be taught, also, how to examine his own urine and how to estimate the intake and output of carbohydrate.

Eventually the caloric intake should be so adjusted, if possible, that ketones and sugar do not reappear in the urine and that the patient neither gains in weight nor suffers any progressive loss of weight. Ordinary bread is rarely allowed, but substitutes made of gluten flour of known composition, such as Akoll biscuits, may be used. To fill the stomach bran biscuits[1] may be ordered. Tea, coffee, gelatin jellies, etc. may be sweetened, if necessary,

[1] The recipe used at the Rockefeller Institute Hospital is:

| | |
|---|---|
| Bran | 60 gm. |
| Salt | ¼ teaspoonful |
| Agar-agar, powdered | 6 gm. |
| Cold water | 100 mils (½ glass) |

Tie bran in cheese cloth and wash under cold water tap until water is clear. Mix agar agar in the water (cold) (100 mils) and bring to the point of boiling. Add to washed bran the salt and agar-agar solution (hot). Mold into three cakes. Place in pan and, when firm and cold, bake in moderate oven from forty-five to fifty minutes.

with saccharin, although the persistent use of this drug sometimes results in indigestion.

No drug has any influence on the course of diabetes. Opium in crude form or its alkaloid codein promotes comfort by obtunding perceptions and may diminish slightly the glycosuria by retarding the absorption of carbohydrates, but its use is inadvisable except in hopeless cases. Tonics are sometimes indicated. Constipation, which is baneful, if not relieved by food substitutes (bran, agar-agar, etc.) must be combated by vegetable or saline cathartics. Courses of bromids are sometimes of service in controlling nervous manifestations. All rules conducive to good health should be followed as closely as possible and especial care should be taken to avoid infections, even common "colds."

Most of the complications of diabetes are controlled or greatly benefited by strict dieting. Diabetes does not modify the usual principles of surgical procedure in such conditions as gangrene and cataract, although operations of all kinds are of course, rendered more dangerous by the disease. If a general anesthetic is required ether and chloroform should be avoided and nitrous oxid-oxygen employed. Boils usually yield to vigorous antidiabetic treatment. Pruritus of the genitals may be relieved by anointing the parts freely with petrolatum before urination or protecting them with zinc stearate. General pruritus may require the use of a wash containing phenol, resorcinol or boric acid (see p. 500). The treatment of diabetic coma is considered on page 387.

## DIABETES INSIPIDUS

**Definition.**—Diabetes insipidus is a chronic disease characterized by the excretion of large quantities of dilute urine, free from sugar and other abnormal constituents, accompanied by polydipsia but not by any increase in the general arterial pressure. It was first clearly distinguished from diabetes mellitus by Willis in 1674.

**Pathogenesis.**—The nature of diabetes insipidus is obscure, but the well known observation of Claude Bernard that puncture of the floor of the fourth ventricle close to the "glycosuric center" produces simple polyuria, the discovery of the diuretic action of extracts of the posterior lobe of the pituitary body by Magnus and Schaefer,[1] the success of Camus and Roussy[2] in producing polyuria by injuring the pituitary body or the brain in the immediate neighborhood of it, and the numerous reports of cases in which diabetes insipidus has occurred in association with coarse lesions of the brain involving the pituitary body and of cases of diabetes insipidus in which injections of pituitary extract have afforded symptomatic relief, leave little room for doubt that in many instances, at least, the disease is dependent upon some disturbance of the pituitary body, probably lowered functional activity of its posterior lobe.

That other explanations may hold in some cases is not unlikely. The studies of Talqvist,[3] Meyer,[4] Seiler[5] and others favor the hypothesis that diabetes insipidus is sometimes due to the inability of the kidneys to excrete

[1] Jour. of Physiol., 1901, 1902.
[2] Presse médicale, 1914, xxiii, 5–17.
[3] Zeit. f. klin. Med., 1903, xlix.
[4] Deutsch. Arch. f. klin. Med., 1905, lxxxiii.
[5] Zeit. f. klin. Med., 1907, lxi.

urine of ordinary concentration, the normal quantity of solids escaping only when such an amount of water is taken that the urine is made abnormally dilute. These observers found that the percentage of different substances in the urine in diabetes insipidus varies but little with changes in diet, although the amount of urine is in direct relation to the character of the diet, increasing with the quantity of solid matter passing through the kidneys. In other cases still, it is possible that polydipsia of cerebral origin is the primary factor and that the polyuria is secondary.

**Etiology.**—Diabetes insipidus is a comparatively rare disease. Thirty-four cases were found in 370,000 patients at the Mayo Clinic[1] and 7 cases in 403,535 patients in the Johns Hopkins Hospital.[2] It is most common in early adult life, although it is relatively frequent in children. Of 124 cases analyzed by Stoermer[3] 15 per cent. of the patients were less than 10 years of age and 9.6 per cent. were under 5 years. Occasionally the disease appears to be congenital. Heredity sometimes plays an important part; thus, in a family cited by Weil[4] there were no less than 35 cases in 5 generations of a family of 219 individuals. Lancereaux has reported 11 cases of hereditary transmission and van der Heidjen[5] 10 cases. Trauma of the head and even severe concussion of the brain may act as an exciting cause. Syphilis is an indubitable etiologic factor in a considerable proportion of cases. In 1909 Ebstein[6] collected from the literature 17 cases of syphilitic origin. In 36 cases of basilar syphilitic meningitis Oppenheim[7] observed polyuria in 12.

The disease not rarely occurs in association with tumor or conglomerate tubercle at the base of the brain. Simmonds,[8] Miller,[9] Sekiguchi[10] and others have reported cases in which there was a metastatic tumor of the pituitary body secondary to carcinoma of the breast. Cases of acromegaly, of dystrophia adiposogenitalis, and of infantilism of the Lorain or Brissaud type with diabetes insipidus have occasionally been observed. Finally, it is said that the disease in rare instances has supervened on diabetes mellitus and that still more rarely the latter has been followed by diabetes insipidus.

**Morbid Anatomy.**—Apart from the cerebral lesions that have already been mentioned and which are not present in all cases, there are few changes directly referable to the disease itself. Dilatation of the renal pelves and ureters and hypertrophy of the bladder, from the undue pressure of the urine, have been observed in some instances. Even though enormous quantities of fluid are often taken for years hypertrophy of heart is not observed in uncomplicated cases.

**Symptoms.**—The disease is characterized by habitual polyuria and excessive thirst and may begin suddenly or gradually. The quantity of urine is usually greater than in diabetes mellitus and may reach 10 or 15 liters (20–30 pints) in the twenty-four hours. In a few cases it has exceeded 20 liters (40 pints) a day. The urine is pale, of low specific gravity (1001–1008), and usually free of abnormal ingredients. Occasionally, it contains small quantities of inosite or muscle sugar. Although the percentage of urinary solids is diminished, the total daily output may be slightly increased.

The thirst is proportionate, as a rule, to the polyuria, but at times, espe-

[1] Rowntree, Med. Clin. of N. America, Sept., 1921.
[2] Futcher, Trans. Assoc. Amer. Phys., 1904, xix.
[3] Quoted by Gerhardt, Nothnagel Spec. Path. u. Therap., vii, I.
[4] Deutsch. Archiv. f. klin. Med., 1908, xciii.
[5] Quoted by Schulmann, Revue de Med., 1920, 37, No. 11.
[6] Deutsch. Arch. f. klin. Med., 1909, xcv, No. 1.
[7] Quoted by Frank, Berlin. klin. Woch., 1912, xlix, 393.
[8] Münch. med. Woch., 1914, lxi, 180.
[9] Amer. Jour. Med. Sci., 1916, cli, 549.
[10] Annals of Surg., 1916, lxiii, 297.

cially in the early stages, more water may be excreted than is drunk, the excess being drawn from the tissues. The patient frequently complains of dryness of the skin and mouth, constipation, lumbar pains, and interruption of sleep from distention of the bladder, but otherwise he may enjoy fairly good health. On the other hand, he may become weak, anemic and emaciated in a comparatively short time, especially if the disease is the result of an organic lesion. The appetite is variable, but in some cases it is inordinate.

**Complications** are somewhat infrequent. Bitemporal hemianopsia, sometimes transitory at first, has been observed in a number of instances, particularly in connection with cerebral syphilis. Spanbock and Steinhaus[1] observed diabetes insipidus in 11 of 50 cases of bitemporal hemianopsia. Paralysis of the sixth nerve has also been noted. Impotence may occur. Reversive infantilism has been described. Pneumonia may develop as a terminal infection.

**Diagnosis.**—In *chronic nephritis* the polyuria is rarely as pronounced as in diabetes insipidus, thirst is not often an obtrusive feature, albuminuria, cylindruria, high arterial tension and cardiovascular changes are usually present, and the functional capacity of the kidneys, as shown by the phthalein output and other tests, is commonly reduced. *Hysterical polyuria* is usually paroxysmal and accompanied by other stigmata, such as anesthesia, paralysis, special sense disturbances, etc. In the polyuria of *polycystic disease of the kidneys* physical examination frequently reveals cardiovascular changes similar to those occurring in chronic nephritis and also palpable masses in the region of the kidneys. Roentgenographic studies may be very helpful in diabetes insipidus in determining whether or not a gross lesion of the pituitary body is the cause of the polyuria.

**Prognosis.**—This depends largely upon the nature of the organic lesion that is responsible for the symptoms. In the absence of tumor or tubercle the disease may last for many years. Actual cure is exceptional, but it may occur in syphilitic cases.

**Treatment.**—The patient should have a nutritious but easily digestible diet and should be placed under favorable hygienic conditions. It is not advisable to restrain him much in the matter of drink, except in the evening when the intake of fluid should be reduced so as to avoid interference with sleep. A salt-poor diet is sometimes beneficial. Arsphenamin, mercury and iodids should be given a thorough trial whenever there is evidence of syphilis. Subcutaneous injections of an extract of the posterior lobe of the pituitary body (1 mil once a day) often gives great relief, although the action of the drug rarely lasts more than twenty-four hours. Oral administration is ineffectual. In a case reported by Herrick[2] and in one reported by Graham[3] lumbar puncture was followed by a cessation of the polyuria and other symptoms for several weeks. Among special remedies that have been extolled from time to time may be mentioned valerian (½–1 fluidounce —15–30 mils of the ammoniated tincture daily), ergot (10 minims—0.6 mil of the fluid extract three times a day), strychnin sulphate (1/30 1/20 grain—0.002–0.003 gm. two or three times a day hypodermically), and bromids.

[1] Quoted by Frank, *Loc. cit.*
[2] Archives of Internal Med., July 15, 1912.
[3] Jour. Amer. Med. Assoc., Nov. 3, 1917.

## OBESITY

(Lipomatosis; Adiposity; Fatness)

Obesity is an excessive accumulation of fat in the body. In determining whether the condition is pathologic or not, one must take into consideration not only the age, sex and frame of the individual, but also the effect that the fatty deposit has upon the functions of the body. Fatness is always to be regarded as pathologic whenever it impairs the individual's general health or even lessens his efficiency.

**Etiology.**—Obesity is much more common in women than in men. In some cases heredity plays an important rôle. It may occur at any age, but in the majority of cases it develops toward the close of the fourth or in the fifth decade. It is rare in old age. Race is not without influence, Hebrews, Germans and certain African races being especially prone to corpulency.

In a very large proportion of cases ordinary obesity is directly attributable to overfeeding or to lack of exercise, or to both of these factors combined. In other cases the habitual use of alcoholic drinks, especially of beer or ale, is an important exciting cause. Alcohol supplies energy, thus sparing the fats, and also promotes physical torpor. Moreover, the malt liquors contain in addition to alcohol much nutritive material, the alcohol and extractive matter combined of a quart of beer furnishing about 500 calories. Whether fluids themselves directly influence fat metabolism has not been definitely determined, but drink restriction may do good in obesity by reducing the amount of water in the tissues, thus making the patient more comfortable and better able to take exercise. Some individuals show a remarkable tendency to lay on fat even though they eat little, do considerable work and abstain from alcohol. It is generally assumed that in such cases there is a constitutional low rate of metabolism, but experimental studies fail to show that corpulent persons, without endocrine disturbances, burn up less fat than others. Certain diseases appear to be conductive to obesity. Thus, chlorotic girls are frequently stout; many gouty and diabetic patients are abnormally fat; and not uncommonly a tendency to over-weight first shows itself during convalescence from an acute infection, such as typhoid fever or pneumonia. The exact relation of these conditions to obesity is, however, unknown.

Finally, certain types of adiposity seem to be clearly traceable to functional disturbance of the endocrinous glands, particularly the gonads, hypophysis cerebri and thyroid. Thus, the obesity which is often observed in eunuchs and in women in whom an artificial menopause has been induced may have this origin. There is considerable evidence, also, to show that certain special forms of abnormal fat deposit, such as Dercum's adiposis dolorosa and Fröhlich's adipositas cerebralis, are related in some way to a disturbance of internal secretion.

**Morbid Anatomy.**—The excess of fat occurs chiefly in the regions in which fat is normally found, although its distribution is seldom uniform. Externally, it is usually most marked in the cheeks, neck, breasts, abdominal wall, flexures of the joints, and about the hips. Internally, it accumulates in the mediastinum, mesentery, greater omentum, capsules of the kidneys, and connective tissue between the muscle-fibers. Of the viscera, the heart and liver are most affected. The subpericardial fat may be so greatly increased as to form a thick envelope enclosing almost the entire heart. In extreme cases the fat may even penetrate between the muscle-fibers, causing atrophy of the latter and occasionally true fatty degeneration. The liver is large and of a yellowish color, its edges are rounded, and when incised it

greases the knife-blade. In the cells of the organ large and small drops of fat are seen, many of which push the nucleus aside or conceal it.

As a result of the adiposity both the girth and weight of the body are increased. In well-marked cases the weight may be from 50 to 100 per cent. above what is regarded as normal for an individual of the same height, age and sex as that of the patient. Extreme weights of 500 and even of 700 pounds have been recorded.

**Symptoms.**—The earliest symptoms of obesity are attributable to the increase in the bulk of the body, and consist of a lack of suppleness and of ready fatigue. Owing to the increased exertion that is required to execute necessary movements, there is also a tendency to excessive sweating. These symptoms incline the patient to avoid exertion, and thus a so-called vicious circle is produced, for the lack of exercise weakens the muscles and favors the development of fat. As the obesity increases, breathlessness on exertion becomes a conspicuous symptom. The dyspnea is due to the lessened capacity of the thorax, the excessive thickness of the chest wall, interference with the action of the diaphragm by the abdominal fat, and the increasing disproportion between the muscular strength and the effort required to make any movement of the body. At the same time the circulation becomes affected unfavorably, as shown by increased frequency of the pulse, palpitation, and finally signs of passive congestion. In advanced cases the venous stasis may be sufficient to cause digestive disturbances, bronchial catarrh, oliguria, and edema. As a result of friction and moisture, erythema intertrigo often develops where surfaces of the skin come in contact, as beneath the mammæ, between the buttocks and in the groins. Under the influence of the disease resistance to bacterial infection is usually lessened. In the married state sterility is not an uncommon consequence of extreme adiposity. Gout, diabetes and arteriosclerosis often occur in obese persons, but they are probably referable to the causes of the corpulency rather than to the latter itself. Joslin[1] has pointed out that persons who are from 6 to 20 per cent. above weight are from 6 to 12 times as liable to diabetes as their counterparts in the same group below weight. Cases of simple obesity with one or more of the symptoms of adiposis dolorosa (see p. 382) are occasionally observed.

**Prognosis.**—This depends upon the degree of obesity, the nature of the underlying factors, and the amenability of the patient to the requirements of treatment. Generally speaking, the outlook is relatively favorable in the earlier stages of the disease, particularly if the cause is excess in eating and there is no strong family tendency to fatness.

**Treatment.**—The aim must be to diminish the supply or to increase the destruction of fat. The first aim is accomplished by restriction of food, and the second, chiefly by properly regulated exercise. In whatever direction the effort at reduction is made it must be recognized that a loss of weight in excess of one or at most two pounds a week is, as a rule, undesirable, and likely to be attended with nervous irritability, general weakness or other untoward effects. Especially important is it to see that the loss of proteins does not exceed the supply, at least for any considerable period. During the treatment the patient should be seen at brief intervals, so as to afford frequent opportunities for taking and recording his weight, observing the effect of the reducing process on his general health, and making such modification in the dietetic and other regulations that changes in his condition may require. In arranging the diet an endeavor should be made to diminish the total quantity of nutritious food while at the same time admitting a sufficient

[1] Jour. Amer. Med. Assoc., Jan. 8, 1921.

bulk of palatable material to have a satisfying effect upon the appetite. The ingestion of fats, sugar and starches in particular must be limited, although other foods must also be taken in moderation. Ordinarily the protein content of the diet should not be much less than 100 grams a day.

Green vegetables and tart fruits may be allowed in relatively liberal amounts, as they are bulky in proportion to their caloric content. Of course, the degree of restriction must be determined in each separate case by the results and these are best judged by the weight and subjective sensations of the patient. Ordinarily, the total amount of calories may be safely reduced, at least for a time, to about one-half of that necessary to maintain an individual of the same age and sex as that of the patient, but of normal weight.

The patient must weigh each portion of meat, bread, etc. until he is able to judge accurately the amount that is permissible from its bulk. As a rule, the meals should be limited to three, but occasionally it may be necessary to lessen the appetite by allowing raw fruit or a cup of bouillon in the intervals between meals or on retiring. Water should be restricted in amount and taken preferably between meals. Especially important is it to limit the entire amount of fluid taken in the twenty-four hours when there are indications of cardiac insufficiency.

Special dietetic measures may be of value in certain cases of obesity, if the patient can be kept in bed or at rest. Among these are the various modifications of the milk cure. Thus, a liter of milk may be given on two days of each week, and a more or less restricted general diet during the remainder of the week. Although the various milk cures are virtually starvation diets, they have the advantage of a restriction in the amount of fluids. Complete starvation, which is sometimes resorted to voluntarily by obese subjects, is the most rapid method of reducing weight, but to be perfectly safe it must be in the form of a series of repeated fasts of increasing duration. Uninterrupted starvation is likely to cause within a day or two acidosis with headache, dizziness, nausea, etc. (Folin and Denis.)[1]

Muscular exercise constitutes the best method of promoting the destruction of fat already stored up in the tissues. It must be carefully graded, however, according to the strength of the patient. In many cases a brisk walk after each meal, the distance being gradually increased, is the best form of exercise. It is scarcely necessary to add that vigorous muscular activity makes possible a more liberal dietary. For feeble patients the exercise may have to be limited to massage or passive movements. For robust subjects, cold bathing, followed by vigorous rubbing, is a valuable adjuvant to physical exercise.

Drugs are of minor importance. Thyroid extract is an active reducing agent, but unfortunately it causes a loss of protein as well as of fat. Occasionally, however, it acts well, but its effects must be carefully observed. Generally speaking, it produces the best results in cases of obesity showing evidences of disturbed endocrinous function. Ordinarily, the dose should not exceed 3 grains (0.13 gm.) of the dried gland two or three times a day. In cases apparently on the borderland between ordinary obesity and Fröhlich's adipositas cerebralis (see p. 383) an extract of the anterior lobe of the pituitary gland may be of service. Saline cathartics have no special influence on the metabolism of fat, although they may bring about desirable subsidiary effects through their action on the bowel. When there are evidences of cardiac insufficiency digitalis or strychnin, or both, will often prove useful. Finally, in extreme cases the excision of large pendulous masses of fat may occasionally be advisable.

[1] Jour. Biol. Chem., 1915, xxi, 183.

The following dietary may be taken as an illustralion of what would be suitable at the beginning of treatment for a man who weighs 200 pounds and who should normally weigh 165 pounds.

*Breakfast*

One orange or one-half grape fruit.....about 80 calories
Two eggs, boiled or poached.....about 160 calories
One ounce of wheat bread or rolls with an extremely small amount of butter.....about 110 calories
One cup of coffee, with two teaspoonfuls of milko(not cream) and with one lump of sugar.....about 44 calories

*Dinner*

Three ounces of clear soup.....about 18 calories
Six ounces of lean meat (mutton, veal, beef or chicken), without gravy.....about 342 calories
(Eight ounces of fresh fish—bass, trout, perch or cod—baked or boiled, may be substituted for ~ther meat)
Four ounces of potatoes (white), baked, or boiled, and without butter.....about 95 calories
Two ounces of one of the following vegetables: spinach, string beans, green peas, asparagus, tomatoes, turnips, prepared without butter.
Four ounces of fresh fruit.....about 50 calories

*Luncheon*

Four ounces of lean meat, baked, boiled or broiled, without gravy.....about 190 calories
(This may be replaced by one dozen small raw oysters.)
One cup of bouillon or clear soup.....about 18 calories
Salad or lettuce, celery, or tomatoes, any quantity, with vinegar or lemon, juice, but no oil.....about 31 calories
One ounce of bread with a small amount of butter.....about 108 calories

| Food material | Protein, grams | Fat, grams | Carbohydrate, grams | Calories |
|---|---|---|---|---|
| **Breakfast** | | | | |
| Orange or half grapefruit | 1.2 | 0.3 | 17.4 | 80 |
| 2 eggs | 13.2 | 12.0 | .... | 160 |
| 2 oz. wheat bread or rolls | 2.6 | 0.3 | 15.0 | 75 |
| Butter (small portion) | 0.04 | 5.5 | .... | 35 |
| Coffee | | | | |
| Milk | 0.06 | 0.8 | 1.0 | 14 |
| Sugar, 1 lump | ..... | .... | 7.6 | 30 |
| **Lunch** | | | | |
| Lean meat (4 oz.) | 23.9 | 10.2 | .... | 190 |
| Bouillon (5 oz.) | 3.3 | 0.3 | .... | 18 |
| Lettuce | 0.5 | 0.1 | 0.4 | 9 |
| Tomato (1) | 0.5 | 0.3 | 3.0 | 16 |
| Celery | ..... | .... | 1.4 | 6 |
| Bread | 2.6 | 0.3 | 15.0 | 73 |
| Butter (small portion) | 0.04 | 5.5 | .... | 35 |
| **Dinner** | | | | |
| Clear soup (5 oz.) | 3.3 | 0.3 | .... | 18 |
| Chicken (6 oz.) | 43.1 | 18.0 | .... | 342 |
| Trout (5 oz.) | 49.5 | 10.5 | .... | 300 |
| Potato (1) | 2.5 | 0.1 | 21.0 | 95 |
| Choice of: | 1.1 | | | |
| Spinach | 1.2 | 0.1 | 1.8 | 14 |
| String beans | 38 | 0.1 | 2.9 | 22 |
| Green peas | | 0.2 | 9.8 | 57 |
| Asparagus | 1.0 | .... | 2.0 | 13 |
| Choice of: | | | | |
| Strawberries (4 oz.) | 1.1 | 0.7 | 7.9 | 42 |
| Apple (5 oz.) | 0.5 | 0.5 | 16.0 | 70 |
| Banana (3½ oz.) | 0.8 | 0.4 | 14.0 | 64 |
| | 98.2 | 54.6 | 100.8 | 1273 |

## SPECIAL FORMS OF ABNORMAL FAT DEPOSITS

The following special forms of abnormal fat deposits are recognized: Adiposis dolorosa (Dercum's disease), nodular circumscribed lipomatosis (simple lipoma), diffuse symmetrical lipomatosis, and cerebral adiposity (Fröhlich's syndrome). It is possible that these conditions do not consitute distinct disease entities, but merely variations of a common morbid process. Intermediate forms are frequently observed that cannot be definitely classified in anyone group. Many French writers believe that neuropathic edema (pseudo-lipoma) is also a closely related condition. The etiology of these peculiar types of adiposity is unknown. A nervous origin (trophoneurosis) has been suggested, but the pathologic findings and the general evidence favor the view that the process is due to defective functioning of one or other of the glands of internal secretion.

**Adiposis Dolorosa.**—This condition, which was first named and classified by Dercum,[1] in 1892, is characterized in its typical form by (1) abnormal fat deposits, nodular or diffuse, usually about the arms and trunk, and less frequently about the legs; (2) tenderness over the affected areas, and often pains of a neuralgic or neuritic type, not only in the regions of the fat deposits, but also in the joints and muscles; and (3) asthenia, varying in degree from readily induced fatigue to extreme muscular weakness. Psychic disturbances, rarely amounting to actual insanity, are sometimes observed in

[1] Amer. Jour. Med. Sci., 1892, civ, 521.

advanced cases, and not rarely certain sensory, vasomotor, or trophic phenomena are also present, the most common, perhaps, being paresthesia, anidrosis, transient erythemas, ecchymoses from trivial injuries, bleeding from mucous membranes, and pigmentation of the skin. Many atypical cases are observed, some differing very little from ordinary obesity, and others scarcely distinguishable from multiple lipomata or from diffuse symmetrical lipomatosis. The condition develops usually in middle life and shows a distinct predilection for females. An hereditary neuropathic predisposition has often been noted. At autopsy the most common findings have been changes in the endocrinous glands, particularly the thyroid and the pituitary body, and evidences of neuritis, especially in the nerves of the fat deposits. The course of the disease is protracted and not rarely interrupted by remissions. Death finally ensues from asthenia or some intercurrent disease. *Treatment* is not very satisfactory. Thyroid extract or a combination of thyroid extract and pituitary extract (anterior lobe) is sometimes of considerable benefit, however, in the early stages. Dietetic measures are not likely to be of service unless there is general obesity. Hydrotherapy and massage may be tried.

**Nodular Circumscribed Lipomatosis (Simple Lipoma).**—Single lipomata are not often associated with either local or constitutional symptoms. Multiple lipomata, however, are sometimes accompanied by local tenderness and by various constitutional disturbances, especially nervous symptoms, including neuralgic pains, ready fatigue, nervous irritability, etc., thus bringing the condition into more or less close relationship with Dercum's disease. According to Adami,[1] the huge retroperitoneal and mesenteric lipomata should be regarded as examples of hyperblastosis, dependent upon some internal secretory disturbance, for they merge into the surrounding fatty tissue, respect the normal boundaries, and present none of the characteristics of true independent tumors.

**Diffuse Symmetrical Lipomatosis.**—In this condition the fatty masses, while more or less localized, are not circumscribed or encapsulated but diffuse and are symmetrically distributed. In the large majority of cases the neck is the part especially affected, producing the *Fetthals* of Madelung,[2] although other parts are usually invaded to some extent. Local and constitutional symptoms are, as a rule, absent, but cases presenting some of the features of adiposis dolorosa are occasionally observed. Unlike other forms of lipomatosis the condition occurs chiefly in males.

**Cerebral Adiposity** (see p. 867).—This syndrome, which was first described by Fröhlich, and later named *dystrophia adiposo-genitalis* by Bartels, is characterized by general adiposity, sexual infantilism, mental and physical lethargy, and sometimes increased tolerance to carbohydrates. The pathologic basis of the disorder appears to be a tumor of the hypophysis itself or a lesion at the base of the brain causing by pressure a suppression of the secretory function of the hypophysis, although it is possible that in some instances disturbances of other endocrinous glands may also be concerned in the process.

**Neuropathic Edema (Pseudolipoma).**—These terms have been applied to the circumscribed infiltrations of the skin that rarely occur in hysteria and in certain lesions of the central nervous system and last indefinitely. The swellings, which are usually small and confined to symmetrical regions, resemble edema, but do not pit on pressure. Sometimes they show a change of color, being abnormally pale (white edema of Sydenham) or of a bluish

[1] Brit. Med. Jour., Aug. 16, 1913.
[2] Archiv. f. klin. Chir., 1888, xxxvii, 106.

hue (blue edema of Charcot), and not rarely they are excessively painful. Many French writers (Mathieu, Chuffart, Bucquoy, Potain) believe that the condition is allied to the various forms of lipomatosis, as cases representing various stages in transition from neuropathic edema and true lipoma may be observed.

## INFANTILISM

*Dwarfism* (microsomia) is underdevelopment of the body, both of the skeleton and soft parts. It is not incompatible with normal mental and sexual development. According to Lancereaux, an adult dwarf should not exceed in height 120 cm. (47 inches). The underlying causes, which are not always apparent, are usually present at birth, although they may become operative in early childhood. A *pure dwarf* is a person of small stature, but well formed. The pigmies of Central Africa may be cited as examples. A *deformed dwarf* is a person who is both abnormally undersized and deformed. Achondroplasic dwarfs and rachitic dwarfs are of this type and in each the deformity is the result of a disturbance in the cartilaginous ossification. The achondroplasic dwarf is distinguished by his short extremities ("seal limbs"), trunk of normal size, large globular head, stumpy nose, and "trident" hands. In the rachitic dwarf the characteristic features are a high forehead with prominent bosses, bizarre bends of the long bones and Harrison's sulcus. A rosary and curvature of the spine are common to both conditions.

*Infantilism* is a condition in which the attributes of childhood persist in adult age. It is characterized by mental delay, hypoplasia of the sexual organs, absence or abeyance of the secondary sex characteristics (pubic hair, in the male deepening of the voice, in the female enlargement of the breasts, etc.), and often, but not invariably, a dwarfish stature. The etiology of the condition is frequently obscure, and in the present state of our knowledge even a clinical classification of the cases is scarcely possible. Chronic infections, such as syphilis, uncinariasis, malaria, etc., and intoxications in the parents (alcohol, lead, etc.) are undoubtedly common causes. In another large group of cases infantilism is clearly associated with a loss or a perversion of one or more of the internal secretions. One of the best known forms is cretinism, which is due to a deficiency of thyroid secretion. When typical it may readily be identified by the usual signs of infantilism, in association with a low forehead, broad face, flat nose, thick lips, imbecilic or idiotic expression, protuberant abdomen, spade-like hands, and dry, wrinkled and leathery skin.

Lorain, Brissaud and Frölich have each described special types of infantilism, but these present many features in common and often blend with one another. Disease of the pituitary gland, producing hypopituitarism or probably, in some instances, dyspituitarism, seems to be the important etiologic factor, although it is possible that other glands may also be concerned in the process. In the Lorain type the figure is dwarfed, but well proportioned and with the outlines of an adult, and the intelligence is good. The facial, axillary and pubic hair, however, is wanting and the genital organs, though well formed, are small. Both the type of Brissaud and that of Frölich are characterized by general obesity and hypoplasia of the sexual organs, but in the former the stature is decreased, while in the latter it is

usually normal or somewhat increased. In the Fröhlich type, moreover, there may be mental dulness, somnolence, increased tolerance for carbohydrates, and certain localizing cerebral symptoms. Even acromegaly and gigantism are sometimes associated with hypoplasia of the generative organs (sexual infantilism). In the status lymphaticus a state of infantilism not rarely persists after puberty. Morlat[1] has reported the same association in three cases of Addison's disease.

Under the names ateliosis and progeria Hastings Gilford[2] has described two other forms of infantilism, which are probably the result of faulty internal secretion. Ateliosis is in many respects the antithesis of acromegaly. It is characterized by a childish facial appearance, diminutive stature, with short slender limbs, ill-developed muscular prominences, small jaw bones, a thin piping voice, low arterial tension and scanty urination. Progeria is a curious combination of the attributes of childhood and those of premature old age. The infantilism is expressed in the small stature, slender bones, and absence of facial and pubic hair, and the senility, in the facial appearance, attitude, manner, gray hair, wasted skin and perhaps signs of cardio-arterio-renal fibrosis.

A condition of infantilism is sometimes seen in congenital heart disease and in heart disease occurring in early life (cardiac type). It has been observed most frequently, perhaps, in association with mitral stenosis. Bramwell, Rentoul, Herter and others have described a pancreatico-intestinal type, with persistent diarrhea as an accompaniment, and Lereboullet and other French writers have drawn attention to the occurrence of infantilism as a complication of hypertrophic biliary cirrhosis in young persons. Finally, infantilism is frequently seen in idiocy. Mongolian idiots have a certain resemblance to cretins, but they may usually be distinguished by the obliquely set eyes, soft skin, tapering finger tips, incurving little fingers, and lively disposition.

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## ABNORMAL OVERGROWTH AND PRECOCIOUS DEVELOPMENT

Abnormal overgrowth of the body, both of the skeleton and soft parts (macrosomia), is observed in gigantism and acromegaly. Both of these conditions are due to hyperpituitarism, which developing before ossification of the epiphyses results in gigantism and developing after that event results in acromegaly (see p. 864).

Precocious growth of the body, with or without obesity, may occur in children in association with tumors or hyperplasia of the adrenal cortex, pituitary gland, pineal gland, and ovary or testicle. In males these lesions are usually accompanied also by premature development of the sexual organs and secondary sex characteristics. In females, however, the tendency is rather in the direction of a masculine transformation. True sexual precocity in girls appears to be associated only with tumors or hyperplasia of the ovaries. Glynn[3] in an analysis of 17 cases of adrenal hypernephroma in children found signs of precocious development absent in but one instance. Occasionally obesity is lacking in these cases and the anomalous sexual development is accompanied by a remarkable increase in stature and muscular strength (Herculean type). So-called renal hypernephromas never

[1] Thèse de Paris, 1903.
[2] Trans. Med.-Chir. Soc., 1902, vol. lxxxv and The Practitioner, 1904, lxxiii, 188.
[3] Quart. Jour. of Med., v, No. 18, 1912.

produce abnormalities of sex and growth. Rorschach[1] has collected from the literature 47 cases of tumor of the pineal gland. Many of the male subjects presented giant growth, premature sexual development and hirsuties.

## ACIDOSIS

By acidosis is meant an abnormal reduction of the alkaline reserve in the blood. The blood probably never becomes actually acid during life, but merely less alkaline. The depletion of the alkaline reserve is usually due to an excessive production of acids, but it may also result from a lessened excretion of these substances. The normal reaction of the blood is maintained (1) by the presence of alkaline salts, of which the most abundant is sodium bicarbonate; (2) by pulmonary ventilation, which serves to remove $CO_2$—the acid most abundantly formed in the body; (3) by the excretion of acid by the kidneys, partly in the free state, but mainly in the form of acid phosphate; and (4) by the formation of ammonia from the antecedents of urea and the elimination by the kidneys of acids in the form of ammonium salts. The primary effect of any depletion of the blood in fixed bases is a diminution in its capacity for carrying $CO_2$ and other acids. The accumulation of $CO_2$ in the tissues serves to stimulate the respiratory center, deepen the respirations and increase ventilation in the lungs. As a result of the increased pulmonary ventilation the tension of $CO_2$ in the alveolar air, and hence in the arterial blood, is diminished. The $CO_2$ tension in the alveolar air is, therefore, a measure of the extent to which the alkaline reserve of the blood is depleted. With the continued production of acids in excess the body defenses against acidity (pulmonary ventilation, excretion of acids by the kidneys, etc.) may in time break down and the depletion of fixed bases exceed the body's capacity for replacing them. In this event the blood becomes constantly less alkaline and finally so-called acid intoxication supervenes.

**Causes of Acidosis.**—Acidosis may occur in the following diverse conditions: In starvation, following the continued use of a carbohydrate-free diet, in diabetes mellitus, in the toxemias of pregnancy, in surgical anesthesia, in advanced nephritis, in uncompensated cardiac diseases, in extensive lesions of the lungs, in acute yellow atrophy of the liver, in Asiatic cholera, in diseases associated with marked wasting, in poisoning by various drugs, including the heavy metals, phlorhizin, antipyrin and morphin, and in children in many different diseases, but especially in severe diarrhea, recurrent (cyclic) vomiting, and acute infections. The severe grades of acidosis (acid intoxication) however, are uncommon except in diabetes, the gastrointestinal intoxications of childhood, and some of the nephropathies.

*The Acids.*—The acids responsible for acidosis are not the same in all cases. The acidosis of starvation, meat-fat dieting, diabetes mellitus, surgical anesthesia and cyclic vomiting is due chiefly to an overproduction of acetone bodies—beta-oxybutyric acid, diacetic acid and acetone. On the other hand, the acidosis of nephritis apparently depends on the retention and accumulation in the blood of acid phosphates (Marriott and Howland[2]), while that of certain pulmonary lesions seems to be the result of an excessive accumulation of $CO_2$.

[1] Beiträge z. klin. Chirurg., 1913, lxxxiii, No. 3.
[2] Arch. Int. Med., 1916, xviii, 708.

The acetone bodies are produced by the incomplete oxidation of fatty acids derived either from fats or from amino-acids formed in the cleavage of proteins. By far the larger amount comes from fats. Diacetic acid is formed by the oxidation of beta-oxybutyric acid, although the process may be reversed, beta-oxybutyric acid being formed by the reduction of diacetic acid. The latter by yielding its $CO_2$ forms acetone. The toxic effects of beta-oxybutyric and diacetic acids in excess are due mainly to their acid properties, but it is possible that these acids may also exert a specific effect. Acetone is not an acid and is not markedly toxic.

**Symptoms.**—The milder forms of acidosis can be detected only by laboratory tests. Of the severer forms (acid intoxication), the most characteristic feature is excessively deep respiration ("air hunger") without cyanosis, due to a reduction in the blood capacity for transporting $CO_2$ and the pronounced stimulating effect of this acid in excess upon the respiratory center. In acidosis due to the acetone bodies there is also drowsiness deepening into coma. Headache and vomiting may occur, and in some cases there is a peculiar "fruity" or aromatic odor to the breath.

**Laboratory Tests.**—In acidosis due to excessive production of acetone bodies, acetone, diacetic acid, and beta-oxybutyric acid may be detected in the urine by qualitative tests (see p. 368), but the presence of these bodies in the urine is not in itself proof of actual acid intoxication. Although acetone bodies are excreted in many diseases, their production is not often sufficient to cause serious untoward effects. Large amounts in the urine, however, especially in association with hyperpnea, usually presage coma. On the other hand, if the functional activity of the kidneys is impaired, as not rarely occurs in diabetes, there may be severe acidosis without acetonuria. Again, it must be remembered that in some other forms of acidosis, such as that of renal origin, acetone bodies do not appear in the urine. Acidosis due to acetone bodies may also be detected and roughly measured by estimating the ammonia content of the urine, although this method is defective in that it merely indicates the amount of acid and bases that is being excreted by the kidneys. The alkali tolerance test of Sellards[1] is of considerable value, although it fails in the presence of cystitis with changes in the urinary reaction. It consists in ascertaining the amount of sodium bicarbonate that must be taken by the mouth in order to render the urine alkaline. About 5 gm. suffices in normal adults, but when acidosis is present two, three, or even five times that amount may be required. More accurate methods of estimating the degree of acidosis are the Marriott[2] method of determining the $CO^2$ tension in the alveolar air and the Van Slyke[3] method of determining the bicarbonate content of the blood. The Marriott method, although somewhat less reliable than that of Van Slyke, is comparatively simple and can be carried out in a few minutes.[4]

**Prognosis.**—In general the severer grades of acidosis offer an unfavorable prognosis. Diabetic acidosis with coma is almost invariably fatal. Although consciousness is sometimes restored, the patient very rarely survives for a longer period than a few days or weeks. In the severe acidosis of chronic nephritis the outlook is also very grave. On the other hand, certain acidoses of childhood are frequently recovered from under prompt and appropriate treatment.

**Treatment.**—The first indication is to prevent, as far as possible, the

[1] Bull. Johns Hopkins Hosp., 1912, xxiii, 289.
[2] Jour. of Amer. Med. Assoc., 1916, lxvi, 1594.
[3] Jour. Biol. Chem., 1917, xxx, 347.
[4] Hynson and Westcott (Baltimore) have devised a simple instrument for estimating the tension of the alveolar air.

further production of acids. Thus, in fasting, feeding should be instituted at once or, if coma is actually impending and the patient has been on an ordinary diet, a moderate amount of carbohydrate in the form of thin oat-meal gruel made with water (60 grams of oatmeal each 24 hours for a patient weighing 150 pounds) should be ordered. In the severe acidosis of cyclic vomiting withdrawal of food (except dextrose) and colonic irrigation are important measures. Dextrose is apparently of service in all forms of acidosis except that due to diabetes. It may be given in 5 or 10 per cent. solution by the mouth, by the rectum or intravenously. In children 100 to 200 mils of a 4 per cent. solution, with 2 per cent. of sodium bicarbonate, may be injected intravenously at one time. Irrespective of the nature of acid intoxication, sodium bicarbonate seems to be helpful in replenishing the alkali reserve, although Joslin,[1] believes that it does more harm than good. It may be given by the mouth (4 to 6 grams or more in weak solution every two hours or by the rectum (3 to 5 per cent. solution). In urgent cases, however, it is best given intravenously (not subcutaneously) in 4 per cent. solution made with freshly sterilized water. For an adult 500 mils or more may be injected every few hours. A neutral reaction of the urine or, better, a normal blood $CO_2$ reading, is an indication that sufficient alkali has been given. Solutions of sodium bicarbonate should not be boiled as the heat tends to transform the bicarbonate into carbonate, which is injurious. Whether alkali is used or not, a large amount of fluid (1000 mils within each 6 hours) should be prescribed. The fluid may be taken by the mouth as water, tea, coffee or thin broths, or by the rectum or intravenously in the form of normal saline solution. Nausea must be avoided and every effort that excites it should be suspended. Free evacuation of the bowels is necessary and may be secured by calomel and salts or by enema.

## ALKALOSIS

The term alkalosis is applied to increased alkali reserve, with or without high blood alkali. It is less common than acidosis. It may be produced by the administration of large amounts of alkali, for example, sodium bicarbonate or sodium carbonate. It may occur in pyloric obstruction with exclusion of hydrochloric acid from the duodenum. Wilson,[2] and his co-workers have shown that it follows parathyroidectomy, the equilibrium between acids and bases being displaced by this procedure in favor of the bases. It may also result from voluntary overbreathing or forced respiration, such as occurs during general anesthesia. In this acapnial form there is apparently alkalosis with low blood alkali, for the carbon dioxid of the blood and tissues being abnormally decreased by the respiratory overwork, the alkali reserve becomes relatively high and to meet this a part of the alkali of the blood is withdrawn.

Clinically, the chief manifestation of alkalosis is the occurrence of tetany (see p. 1020).

[1] Joslin: Treatment of Diabetes, Phila., 1917.
[2] Jour. Biol. Chem., 1915, xxi and xxiii.

# DISEASES OF THE DIGESTIVE SYSTEM

## DISEASES OF THE MOUTH, TONGUE, TONSILS, PHARYNX, AND SALIVARY GLANDS

### STOMATITIS

Stomatitis, or inflammation of the mouth, may result from the action of certain chemical poisons, either before absorption, as in the case of strong acids and alkalies, or after absorption, as in the case of mercury, iodids, bromids, etc.; it may be due to the action of mechanical irritants, such as broken teeth, foreign bodies etc., and it may be caused by the action of thermic irritants, such as intensely hot food and drink. In the majority of cases, however, it is of microbic origin, occurring as an independent condition or as an accompaniment of some general infection, such as scarlatina, measles, typhoid fever, syphilis, etc. Various microörganisms are found in the lesions, the most frequent being streptococci, staphylococci, pneumococci, diphtheria bacillus, and fusiform bacillus. Even when the exciting cause is mechanical or thermic irritation, the inflammatory process is often intensified and prolonged by the invasion of bacteria.

Of the various forms of stomatitis, a number occur chiefly in infants or young children, although even to these adults are by no means immune. Insanitary surroundings, improper feeding, failure to keep the mouth clean, gastrointestinal derangements, and debility from preëxisting disease are predisposing factors. Some of the clinical types usually described are closely related etiologically and probably represent merely stages of the same pathologic process.

#### CATARRHAL STOMATITIS

In this form of stomatitis the mucous membrane is red and swollen, and the mouth is hot and painful. Granular elevations due to distention of the follicles are sometimes seen, and in severe cases there is more or less epithelial proliferation and desquamation. The saliva is much increased and owing to its acrid properties, it not rarely causes irritation of the skin around the mouth. General disturbances are usually wanting, except in infants in whom the disease produces restlessness, fretfulness, more or less difficulty in nursing, and sometimes a slight elevation of temperature.

**Treatment.**—The cause must be removed if possible. In infants, cleansing of the mouth and of the mother's nipples, or of artificial nipples, if these are being used, is imperative. Digestive disturbances should receive careful attention. Cool antiseptic mouth-washes, such as a 10 per cent. solution of boric acid with 5 per cent. of glycerin, are serviceable. In obstinate cases the mouth may be lightly painted with a 1 per cent. solution of silver nitrate.

#### APHTHOUS STOMATITIS

Aphthous stomatitis is mostly a disease of infancy, although it is occasionally observed in adults. It is characterized by all the phenomena of a catarrhal process, and in addition by an eruption of small vesicular elevations, which are soon transformed into shallow, grayish or yellowish-white erosions.

The latter appear in successive crops and are seen chiefly on the tongue, on the inside of the lips and cheek, and on the gums. The local symptoms are those of catarrhal stomatitis, but the pain is, as a rule, more severe. The disease usually runs its course in from a week to ten days.

**Treatment** is essentially that of the underlying condition. Locally, a boric acid wash usually suffices. Intractable ulcers may be touched with a 5 per cent. solution of silver nitrate.

## ULCERATIVE STOMATITIS

This form of stomatitis may occur at any period of life, but it is most common in childhood, between the ages of three and ten years. It is seldom seen except in debilitated subjects. It may represent an advanced stage of catarrhal or aphthous stomatitis. It may develop in the course of the acute infections, such as measles, scarlet fever, pertussis, etc. It is common in scorbutus. Some cases are due to the ingestion of metallic poisons, such as mercury, phosphorus, copper, etc. Occasionally, ulcerative stomatitis is the first indication of acute leukemiæ. Outbreaks of the disease sometimes occur in insanitary barracks, jails, asylums, etc. The bacteriologic etiology is not specific, but not rarely the fusiform bacillus and spirillum of Vincent are present.

**Symptoms.**—The disease usually begins about the gums at the bases of the teeth. The affected tissues at first are red, swollen and spongy. Necrosis soon occurs and a linear ulcer with a gray, sloughing base is formed. Occasionally the destructive process penetrates to the periosteum of the jaw or extends to the contiguous portion of the cheek. There is much pain in the mouth, the flow of saliva is excessive, the breath is peculiarly offensive, the submaxillary lymph-nodes are swollen and tender, and the constitutional disturbance is often marked. With appropriate treatment, however, recovery usually occurs.

**Treatment.**—Hygienic conditions should always receive careful attention. The general health of the patient should be improved by dietary measures and, if necessary, by the administration of tonics. In many cases potassium chlorate is almost a specific. The dose for a child of three or four years is from 1 to 3 grains (0.06–0.2 gm.), in dilute solution, every three hours. The official preparation of hydrogen dioxid, diluted with two or three parts of water, makes a good mouth wash. Ulcers may be painted with a solution of silver nitrate (10 per cent.) or tincture of iodin, or, in case of infection with the organisms of Vincent's angina, with undiluted Fowler's solution (three or four times a day) or with arsphenamin (once daily).

## GANGRENOUS STOMATITIS

### (Noma; Cancrum Oris)

This comparatively rare form of stomatitis usually involves the cheek and adjacent parts. It occurs chiefly in children between the second and eighth years and almost exclusively in those who are already debilitated by other disease, most commonly one of the specific infections, especially measles or whooping-cough. Various pathogenic organisms have been found in the tissues, such as pyococci, diphtheroid organisms, the diphtheria bacillus, fusiform bacillus and spirillum of Vincent, and a form of streptothrix.

The disease may supervene upon ordinary ulcerative stomatitis, but very frequently it develops independently. In the latter event the favorite site is the mucous membrane of the cheek near the corner of the mouth. A hard

livid swelling makes its appearance and is soon transformed into a gangrenous ulcer. Outside, the cheek becomes discolored, hard, swollen and edematous. The gangrenous process rapidly spreads and in two or three days often results in perforation of the cheek and destruction of a large part of the face, leaving the cavity of the mouth exposed. Not rarely the teeth loosen and fall out and the maxillary bones become necrotic. An unbearable stench emanates from the mouth, the appetite is lost, the pulse is weak and accelerated, and the temperature, although often high at first, is usually subnormal before death. Owing to destruction of the nerve filaments there is comparatively little pain and owing to extensive thrombosis of the vessels hemorrhage is rare. The mortality is very high, at least 75 per cent. of the cases terminating fatally in from ten days to two weeks from aspiration pneumonia, sepsis and exhaustion, or intractable diarrhea. When recovery occurs, it is usually with marked deformity from cicatrization.

**Treatment.**—The disease tissue should be destroyed under anesthesia with the actual cautery or nitric acid. After the operation the mouth should be cleansed at frequent intervals with a solution of hydrogen dioxid (1 : 3) or of potassium permanganate (1 per cent.). Externally, wet dressings of Carrel-Dakin solution or of diluted alcohol should be employed. If diphtheria infection is proved by culture, diphtheria antitoxin should be used. Concentrated nourishment and general stimulants are indicated.

## THRUSH

### (Mycotic Stomatitis)

Thrush is a form of stomatitis due to a pleomorphic yeast-like fungus, *Oïdium albicans*, and characterized by the appearance of small white patches on the buccal mucous membrane. It occurs chiefly in young infants who are improperly fed and cared for, although it is occasionally observed in older children, and even in adults, who are greatly debilitated by other disease.

The appearance of the mouth is characteristic, the mucous membrane presenting more or less numerous small, opaque, white patches, resembling flecks of curdled milk. If the disease is neglected the patches may coalesce and form a membrane. The growth is firmly adherent and if removed forcibly leaves an abrasion. Microscopic examination of the detached tissue shows interlacing mycelia or ovoid yeast-like-cells. Symptoms of catarrhal stomatitis are always present and in many cases there are coincident gastrointestinal disturbances. The mouth is, as a rule, the only part infected, but occasionally the lesions spread to the tonsils, pharynx and esophagus. In comparatively healthy children thrush usually yields to appropriate treatment within a week or ten days.

**Treatment.**—After each feeding the affected parts should be treated gently but thoroughly with a saturated solution of boric acid or a solution of sodium bicarbonate, 10 grains to the ounce (0.65 gm. to 30.0 mils). The applications may be made with absorbent cotton or a soft piece of rag wrapped around the index finger. To prevent reinfection the mother's nipples, or if the infant is bottle-fed, both the nipple and the bottle must be thoroughly cleansed before and after each feeding. If there is disorder of the digestive tract, suitable treatment should be instituted.

## OTHER FORMS OF STOMATITIS

**Gonorrheal stomatitis** sometimes occurs in new-born infants as a result of infection of the mouth with the gonococcus during birth. It has also

been observed in adults. It is characterized by catarrhal inflammation and the formation of a whitish deposit on the tongue, gums and cheeks. It usually yields readily to applications of silver nitrate (1 to 2 per cent.). **Membranous stomatitis** is usually a manifestation of diphtheria, but it is observed also in Vincent's angina, and it may result from the action of pyogenic organisms and of corrosive poisons. **Mercurial stomatitis** (mercurial ptyalism) may occur from the constant handling of metallic mercury, but much more frequently it is observed as an effect of excessive mercurial treatment. It is described on p. 333. **Bednar's aphthæ** is the name applied to a rare affection of new-born infants consisting of yellow or grayish areas of necrosis or ulceration on the posterior part of the hard palate, one on each side of the median raphe. The aphthæ are ascribed to violence in cleansing the mouth or to friction of a long rubber nipple. **Riga's disease** is an ulcerative lesion, followed by a papillomatous growth, on the lingual frenum of infants. It is probably due, at least in part, to injury of the frenum by the lower incisor teeth. It seems to have been observed chiefly in Italy.

**Perléche** is an infectious disease of the labial commissures, occurring chiefly in children, and characterized by thickening and maceration of the epithelium and the formation of fine transverse fissures. It is attended by very little inflammatory reaction and does not proceed to ulceration. The disease is highly contagious and is probably caused by a streptococcus. It must be distinguished from the mucous patches of syphilis, which it may closely resemble. Applications of a 10 per cent. solution of silver nitrate or of a 5 per cent. solution of chromic acid usually effect a cure in a few weeks.

## ACUTE GLOSSITIS

**Acute catarrhal glossitis,** or acute inflammation of the mucous membrane of the tongue, is usually observed in association with acute stomatitis. **Acute parenchymatous glossitis** is a more serious condition, but is rare. It may be caused by trauma, scalds, bites of insects or caustic drugs. It may also occur in certain intoxications, as by mercury or iodides. The tongue is painful, red, and greatly swollen, and there are often systemic signs of acute infection. Mastication, articulation and deglutition are painful and at times impossible. Suppuration may ensue.

**Treatment.**—Antiseptic mouth washes, cracked ice, and applications of cocain and epinephrin are beneficial. Superficial scarification will sometimes relieve intense congestion and edema, but free incisions should be made when the presence of pus is suspected.

## CHRONIC GLOSSITIS

Chronic glossitis results from long-continued irritation of the tongue, as by jagged teeth, alcohol, tobacco, etc. It may also arise from chronic gastro-intestinal disorders and chronic systemic conditions, such as syphilis, diabetes and severe anemia. The tongue is red, hypersensitive, and often abnormally smooth, especially in certain areas, owing to atrophy of the papillæ. In other cases the organ is deeply fissured or the seat of superficial ulcerations (glos-

sitis dissecans). **Treatment** consists in removing the underlying cause, using antiseptic mouth washes, and applying to the affected parts a solution of silver nitrate (2–5 per cent.).

## GEOGRAPHIC TONGUE

This comparatively rare condition, known also as eczema of the tongue and ringworm of the tongue, is characterized by hyperplasia and desquamation of the superficial epithelium of the tongue, with the formation of irregular circinate patches, which are red and smooth in the center and grayish-white and slightly raised at the periphery. The lesions spread at the margins while healing in the center, and tend to involve successively different parts of the tongue. The disease occurs most frequently in infants and is of unknown origin. It may persist for months or years and is prone to relapse. **Treatment** consists in correcting any constitutional or digestive disorder that may be present, in using antiseptic mouth washes, and in applying silver nitrate in solution (2 per cent.). The administration of arsenic is sometimes of benefit.

## LEUKOPLAKIA

Leukoplakia is a disease of the buccal mucous membrane, most frequently involving the tongue, characterized by the development of rounded or irregularly shaped patches, of a milk-white or pearly white color, slightly thickened, stiff, and sometimes bounded by a line of hyperemia. The disease is chronic and resistant to treatment. After reaching a certain stage, the patches may remain more or less stationary, but in some cases they become very thick and show a tendency to crack, and in this event ulceration and epitheliomatous degeneration are likely to supervene.

The cause of the disease is not definitely known. Syphilis and excessive smoking are generally believed to be predisposing factors. In some cases the buccal lesions are associated with affections of the skin, especially psoriasis. Whatever may be the original cause, all authorities agree that the condition is aggravated by smoking, alcohol, hot and pungent foods, irritation by rough and jagged teeth, and various gastro-intestinal disorders. In the **treatment** the removal of all sources of irritation is of the first importance. Tobacco and alcohol must be absolutely forbidden. In the early stages mild alkaline mouth washes and occasional applications of glycerite of tannin may be of service. When there is much epithelial thickening, however, the only treatment that is likely to be effective is by thermocauterization or the röntgen ray.

## ULCERATION OF THE TONGUE

Ulceration of the tongue may be evidently simple, the result of disorders of the digestive tract or, more commonly, of irritation caused by a jagged tooth or salivary calculus, or it may be syphilitic, carcinomatous, or tuberculous.

**Simple ulcers** are characterized by absence of neuralgic pain, of induration, and of lymphatic enlargement, and heal promptly when the exciting cause is removed.

**Syphilitic ulcers** of the tongue are comparatively rare and are usually accompanied by other evidences of syphilis. They are often multiple and symmetrical; they are not attended by enlargement of the regional lymph-nodes; they are relatively painless, and they rarely interfere with the mobility of the organ.

**Carcinomatous ulcers** are relatively common and vie in frequency with carcinoma of the lower lip and esophagus. They occur chiefly after the fortieth year, and more than 85 per cent. of the cases are in men. Long-continued irritation or ulceration of any kind strongly favors their occurrence.

The lesion is solitary, and usually on the side of the tongue, although any part of the organ may be affected. It is, as a rule, surrounded by an area of induration; it is usually very painful; it interferes with the mobility of the tongue, and it is accompanied by enlargement of the submaxillary lymph-nodes. Whether these characteristics are present or not, however, any ulcer of the tongue which occurs in a person over 40 and which does not yield promptly to simple treatment should arouse suspicion and should be investigated microscopically.

**Tuberculous ulcers** of the tongue are very rare and usually associated with advanced pulmonary tuberculosis. They may occur on any part of the tongue, but the tip and edges are the favorite sites. As a rule, they are shallow and without surrounding induration, are only slightly painful, and are unaccompanied by enlargement of the regional lymph-nodes.

## BLACK TONGUE

This rare condition is characterized by the development of a blackish, bluish, or greenish discoloration of the dorsum of the tongue, beginning immediately in front of the circumvallate papillæ and extending some distance toward the tip. Accompanying the discoloration there is often, but not invariably, a marked elongation of the filliform papillæ, giving the tongue a curious hairy appearance. Slight discomfort is sometimes experienced as a result of the papillary hypertrophy. A number of microörganisms have been found in the lesions, but the cause of the disease is obscure. The affection is rebellious to treatment and often persists for months or years. Sooner or later, however, it usually disappears spontaneously. Glycerite of tannin and a saturated solution of sodium hyposulphite have been recommended as local applications. The filliform projections may be removed temporarily by scraping.

## MACROGLOSSIA

Macroglossia is enlargement of the tongue due to a lymphangioma, a hemiangioma, or, rarely, simple hyperplasia of the lingual muscle. It is observed chiefly in cretinism, myxedema, and acromegaly, but it may occur as an independent condition.

## ACUTE TONSILLITIS

(Acute Sore Throat; Acute Angina)

Acute inflammation of the tonsils is of frequent occurrence. It is almost always associated with acute pharyngitis. The inflammatory process may affect little more than the mucous membrane, but very often it extends into the follicles or lacunæ, filling them with a yellowish-white exudate, consisting of epithelial detritus, leucocytes and bacteria, and sometimes it involves the deeper tissues of the gland, producing a cellular infiltration, which, if pronounced, usually results in suppuration.

**Etiology.**—Tonsillitis may occur at any age, but it is most common in adolescence and early adult life. It may be the result of mechanical, chemical, or thermic irritation, but in the vast majority of cases it is caused by infection, and is transmissible from one person to another. Chilling of the body favors its occurrence, especially when the system is debilitated or the throat is congested from improper use of the voice. Not rarely the disease prevails epidemically, the outbreaks in some instances being traceable to milk infection. Tonsillitis is frequently the initial manifestation in certain specific infections, such as scarlet fever and diphtheria, and it may be the forerunner of acute rheumatism, of chorea, or of streptococcus septicemia, the tonsils themselves sometimes being the portals of entry for the microörganisms of these diseases. One attack of tonsillitis predisposes to another.

The bacteria most frequently found in the infection belong to the streptococcus group, but staphylococci and pneumococci are sometimes present. Many cases of a mild type, but with a tendency to frequent recurrences and to chronicity, are due to the Streptococcus viridans.

**Symptoms.**—Clinically, three varieties of tonsillitis may be distinguished: Catarrhal, follicular, and phlegmonous (quinsy). The general symptoms do not differ materially in the three forms, although, as a rule, they are mildest in catarrhal tonsillitis and most severe in phlegmonous tonsillitis. The onset, which is often abrupt, is usually marked by chilliness or an actual chill, headache, pains in the back and limbs, and fever. The temperature frequently rises to 102° or 103° F. and may reach 105° F. Swallowing causes pain, the voice is muffled or nasal, the breath is unpleasant. There is a tendency to cough or hawk, a sense of stiffness and soreness is often experienced in the neck, and the submaxillary lymph-nodes are tender and at times moderately enlarged. In follicular tonsillitis an erythematous rash is occasionally observed on the skin.

Local examination reveals a somewhat heavily coated tongue and more or less general redness and edema of the throat. In the *catarrhal form* the tonsils—often one gland more than the other—are congested, swollen and covered with a thin layer of mucoid or mucopurulent secretion. In the *follicular form* the tonsils present, in addition to catarrhal alterations, scattered yellowish-white spots, which represent the lacunæ or crypts of the glands filled with exudate. Frequently the exudate can be expressed by gentle pressure. The spots may remain discrete, or several may coalesce and the tonsil appear to be covered with a false membrane, resembling that of diphtheria. In some of the more severe streptococcus infections a membranous inflammation actually occurs. After subsidence of the inflammatory process the contents of the lacunæ may remain and be transformed by inspissation into cheesy material having a characteristic unpleasant odor. Pellets of this material are sometimes extruded in hawking.

In *phlegmonous tonsillitis* both glands are affected, but usually an abscess forms only in one. The tonsils are greatly swollen, sometimes meeting in the

median line. Speech is interfered with and swallowing is almost impossible. In two or three days, however, a spot of softening appears, and, if incision be withheld, the abscess soon ruptures spontaneously. With the discharge of the pus the symptoms are relieved almost immediately and recovery is thenceforward rapid. In many cases the abscess is in the peritonsillar tissues rather than in the tonsil itself.

**Course and Events.**—Acute tonsillitis, as a rule, terminates in recovery, and even the most severe cases usually run their course within ten days. Chronic tonsillitis with latent, often unsuspected, foci of infection within the glands is, however, a frequent sequel, and moreover there is always the possibility that the infecting organisms will escape from the tonsils into the general circulation and set up inflammatory foci in other parts of the body. Systemic infection by way of the tonsils is, indeed, very common and is particularly characterized by rheumatic and other forms of arthritis, endocarditis and acute nephritis. In children, tonsillitis is probably, the most frequent cause of acute hemorrhagic nephritis. The latter usually follows a week or ten days after the throat symptoms have subsided and may be revealed chiefly by hematuria. Occasionally great numbers of streptococci are suddenly discharged into the bloodstream from an infected tonsil and severe, even fatal, general septicemia supervenes. Local complications may also occur. Thus, there may be an extension of the infectious process to the middle ear, and very rarely in tonsillar or peritonsillar abscess death results from perforation of a large bloodvessel, from thrombophlebitis of the internal jugular vein, or, as in a case cited by Stokes, from the escape of pus into the larynx and suffocation.

**Diagnosis.**—Follicular tonsillitis must not be mistaken for diphtheria, Vincent's angina, or scarlet fever. In *diphtheria* there is commonly a well-defined false membrane of a dirty, grayish-white color. This membrane soon spreads, as a rule, from the tonsils to adjacent structures; it is firmly attached to the underlying tissue, and if forcibly removed leaves a bleeding surface and tends to reform. In follicular tonsillitis there is usually no distinct membrane, but in its stead a collection of yellowish-white deposits, which are confined to the tonsil and which can readily be removed with a swab without leaving a raw surface. However, in many cases the two diseases cannot be differentiated without a bacteriologic examination, for diphtheria may occur without false membrane and, on the other hand, streptococcus tonsillitis is sometimes productive of a membranous formation that is clinically indistinguishable from that commonly found in diphtheria.

*Vincent's angina* resembles diphtheria more than follicular tonsillitis. It may be identified by detecting numerous fusiform bacilli and typical spirilla in smears from the lesions. *Scarlet fever* may usually be distinguished by the history of exposure, the initial vomiting, the very prominent lingual papillæ (strawberry tongue), and the diffuse, bright red, punctate eruption; but there are cases in which the diagnosis cannot be made with certainty.

**Treatment.**—In all but the mildest cases the patient should remain in bed. Isolation is always desirable, and when there is a suspicion that the case is one of diphtheria or scarlet fever it is imperative. A mild aperient is indicated at the outset. The sucking of ice affords relief. The most reliable internal remedies are the salicylates. These should be given in full doses at frequent intervals.

℞. Tricturæ aconiti..... ♏xl ( 2.5 mils)
Sodii salicylatis..... ʒiss ( 6.0 mils)
Syrupi aurantii..... fʒi (30.0 mils)
Aquæ..... q. s. ad fʒiii (90.0 mils).—M.
Sig.—A dessertspoonful every two or three hours.

If given early, biniodid of mercury—$\frac{1}{200}$ gr. (0.0003 gm.) in water every hour for five hours—is sometimes useful, especially in follicular tonsillitis. Occasionally the pain is so severe as to require the use of morphin.

*Local Treatment.*—Externally cold applications often afford more relief than fomentations. Mild antiseptic solutions, such as Dobell's solution or a solution of hydrogen dioxid (1 : 4), are beneficial. Direct applications to the surface of the glands of dry sodium bicarbonate, of finely powdered aspirin, or of the tincture of ferric chlorid are often useful.

℞. Potassi chloratis..... gr. xx ( 1.3 gm.)
Tincturæ ferri chloridi..... f℥iii (12.0 mils)
Glycerini..... f℥iv (15.0 mils)
Aquæ.....q. s. ad f℥ii (60.0 mils).—M.
Sig.—Use locally.

When the swelling is pronounced, scarification, followed by gargling with hot water, is another measure that sometimes affords relief.

Pus should be evacuated as soon as its presence can be detected. In the large majority of cases it is best to make the incision not in the tonsil itself, but in the soft palate, a little above and to the outer side of gland, or at the intersection of an imaginary line drawn horizontally across the base of the uvula and one drawn vertically along the anterior faucial pillar.

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## CHRONIC TONSILLITIS

### (Chronic Hypertrophy of the Tonsils)

**Etiology.**—Chronic tonsillitis is an exceedingly common condition. It is usually the result of repeated attacks of acute tonsillitis. The latter are often so mild that they attract little attention. Probably in some instances the disease begins as a chronic process. The age of occurrence is, as a rule, between the third and fifteenth years, although in many cases the lesions are not recognized until adult life. A lowered vital resistance is an important predisposing factor. Children in whom the lymphatic constitution (lymphatism) is well marked are especially susceptible.

Chief among the bacteria found in the lesions are the streptococci (hemolytic and non-hemolytic), but staphylococci, pneumococci, tubercle bacilli, diphtheroid organisms, etc. are sometimes isolated.

**Morbid Anatomy.**—The tonsils are usually, but by no means invariably, enlarged. They are rough and irregular on the surface, and their lacunæ are often dilated and filled with offensive cheesy material. Sometimes from calcareous infiltration of this material concrements are formed. Incision of the glands may disclose collections of pus of varying size. Fusion of the tonsil with one or the other faucial pillar is not uncommon. Histologically, there is both an increase in the number of lymphoid cells and an overgrowth of connective tissue, sometimes the one and sometimes the other alteration predominating. In some cases the tonsils are unusually small. The reduction in size has been ascribed to shrinking of the overgrown connective-tissue reticulum, but fibrosis is often lacking in the small tonsils and marked in the large ones. In children chronic enlargement of the tonsils is almost always accompanied by overgrowths of lymphoid tissue in the nasopharynx, or so-called adenoids. Indeed, the signs of disturbed physical and mental development which were formerly attributed to enlarged tonsils depend

less upon the latter, as a rule, than upon adenoid vegetations in the nasopharyngeal vault.

**Symptoms.**—Symptoms referable to the tonsillitis itself may be unobtrusive. In many cases, however, the condition is characterized by uncomfortable sensations in the throat, an offensive breath, hypersecretion of mucus, slight cough and a marked tendency to "colds" and sore throat. Local examination may reveal the coarse changes in the tonsils described under Morbid Anatomy, although frequently the signs of infection are less pronounced, and consist merely in a congested, edematous appearance of the glands, with some distortion of the crypts and erosion of the epithelium about their orifices. Even when the surface indications are equivocal, it is frequently possible to express pus from the crypts by making pressure upon the faucial pillar from below against the ramus of the jaw. The size of the tonsils is no criterion, small buried glands often being more dangerous than large ones with plugged crypts. To bring the tonsils into view it is necessary to depress the tongue and, in many cases, to make the patient gag. The diagnosis of adenoids is made by digital examination or, when feasible, by means of the rhinoscope.

The local symptoms of tonsillitis are of little importance compared with the serious secondary conditions which the disease often produces. For example, many cases of rheumatism, of arthritis deformans, of endocarditis, of myocarditis and of glomerulonephritis can be traced to chronic focal infection in the tonsils. Chronic tonsillitis is also an important cause of otitis media and of cervical adenitis, both tuberculous and simple. In about 5 per cent. of the cases of chronic tonsillitis the infection is tuberculous. Diseased tonsils increase the liability to diphtheria and probably also to scarlet fever. Finally, when the disease occurs in young children and is associated with adenoids it commonly results in distinctive physical and mental changes. These depend upon deficient oxygenation from obstruction to the respiration, upon the absorption of bacterial products from the nasopharynx, and possibly in part upon disturbances of internal secretion, for some authors believe that there is some relation between the lymphoid tissues of the pharynx and the endocrinous glands. The child breathes through the mouth, not only when awake but during sleep, and consequently snores and is restless. Night-terrors are common. There is a persistent nasal discharge, cough is frequently present, the breath is foul, the voice is nasal and thick, hearing is often defective, the mind is sluggish, the general health is poor and the resistance to bacterial infection is low. After a time a characteristic facies develops; the expression is dull or stupid, the nostrils are small, the nasolabial folds are marked, and the mouth is kept partly open. Ultimately, even the chest may become deformed, the changes resembling those seen in rickets or less frequently those occurring in emphysema.

**Treatment.**—The only treatment of septic tonsils is complete tonsillectomy and this operation is especially advisable if there are evidences of secondary infection elsewhere in the body or the patient's general health is becoming affected. It is contraindicated, however, during the course of superimposed acute tonsillitis. Treatment by astringent and antiseptic applications invariably fails and incomplete tonsillectomy may aggravate the local condition and favor dissemination of the infection. Pharyngeal adenoids must also be removed by operation. In addition, it is usually necessary to apply general hygienic measures and to administer tonics, such as iron, arsenic and cod-liver oil, so as to increase the patient's vigor and resistance.

## ACUTE CATARRHAL PHARYNGITIS

Acute catarrhal pharyngitis usually occurs in association with acute tonsillitis, and is rare as an independent condition. It gives rise to soreness in the throat, a sense of dryness and tickling and a tendency to hawk and cough in order to remove the mucous secretion. The voice is husky and swallowing is attended with discomfort or actual pain. Upon inspection the throat is found to be red, more or less swollen and covered here and there with thick mucus. The constitutional disturbance is usually slight. The **treatment** is that of acute tonsillitis.

## CHRONIC PHARYNGITIS

Chronic pharyngitis may result from repeated attacks of acute pharyngitis, from overuse of the voice, or from the prolonged action of irritants, particularly tobacco and alcohol. Impairment of the general health favors its occurrence. It is often associated with chronic catarrh of the nose and disorders of digestion. Simple catarrhal, follicular and atrophic forms are recognized, but these tend to merge into one another.

Subjective symptoms are not always present; in many cases, however, the voice is husky and its use is followed by distress; secretion is increased, so that there is a constant tendency to clear the throat; and uncomfortable sensations, as of fulness, dryness or tickling, are experienced. In the catarrhal form inspection of the affected mucous membrane reveals hyperemia, dilatation of the smaller vessels and patches of thick, viscid mucus. The fauces are relaxed and the uvula is elongated. In the follicular form (clergyman's sore throat) the surface is red and studded with more or less numerous elevations, which correspond to the distended follicles. Small superficial ulcers are occasionally seen. In the atrophic form the mucous membrane is pale, smooth, glossy and dry.

**Treatment.**—Removal of the cause is of prime importance. All sources of local irritation, such as overuse or misuse of the voice, mouth-breathing, excessive smoking and intemperance in eating and drinking, must be avoided. Patients should be instructed to expel sounds by the aid of the diaphragm and abdominal muscles instead of the muscles of the throat. Nasal obstructions and adenoid growths must be removed. The habit of hawking and scraping to clear the throat should be rigidly interdicted. Digested disturbances should receive careful attention. Tonics are sometimes required.

The nasopharynx should be kept clean by the local use of mild antiseptic alkaline solutions. Astringent applications, such as silver nitrate—5 or 10 grains to the ounce (0.3–6 gm. to 30.0 mils) or zinc sulphate 5 grains to the ounce (0.3 gm. to 30.0 mils) are sometimes of service. In the follicular form it is advisable to destroy the enlarged follicles by means of the galvanocautery before making use of the astringent applications.

## EPIDEMIC STREPTOCOCCUS SORE THROAT

### (Septic Sore Throat)

During the last two decades epidemics of sore throat due to infection conveyed by milk have occurred somewhat frequently in various communities in England and America. In Boston (1911) 1400 persons were affected; in

Chicago (1911–12), 10,000. The cause of the infection is a peculiar type of hemolytic streptococcus, which is discharged from the inflamed udder of the cow into the milk. It is probable that the infection is primarily of human origin and is transferred to the udder ducts from the hands of a milker suffering from tonsillitis. It is possible, also, that milk may sometimes be contaminated accidentally by human carriers after it has been drawn from the cow. In the course of epidemics secondary cases may develop from contact infection.

After a period of incubation of from 1 to 3 days, the disease begins suddenly with a chill, headache and general muscular soreness. Vomiting may also occur. The temperature rises rapidly and may reach 104° or 105° F. In severe cases there is marked prostration. Locally, the appearances are those of acute follicular or phlegmonous tonsillitis. Pseudomembranous formation may or may not occur. The cervical lymph-nodes are almost always swollen and tender.

In mild cases the acute symptoms usually subside in from 3 to 5 days, but complications are common and may prolong the course indefinitely. Relapses are also frequently observed. The mortality in recent epidemics has varied from 2 to 5 per cent. The most important complications are suppuration of the cervical lymph-nodes, erysipelas, otitis media, bronchopneumonia, general peritonitis, arthritis, pleurisy, nephritis and endocarditis.

Prophylaxis consists in careful inspection of cows and dairy employes and thorough pasteurization of the milk. The treatment is that suggested for acute tonsillitis.

## VINCENT'S ANGINA

Vincent's angina is an infectious, mildly contagious, ulceromembranous disease of the mucosa, usually confined to the tonsils, but sometimes involving the pharynx, the mouth and even the larynx, trachea and bronchi. Two organisms are constantly present in the lesions, one the *Bacillus fusiformis*, a slender rod, slightly swollen in the middle, pointed at both ends, and when stained exhibiting transverse markings; the other a long, actively motile spirillum. It is probable that these two forms represent different stages in the evolution of the same organisms, although it is possible that they are distinct and are merely associated in some symbiotic relation. Infection is favored by a neglected state of the mouth and all conditions that reduce the general strength and vitality. Sometimes it is secondary to other infections, such as diphtheria, measles, scarlet fever, and syphilis. During the recent war the disease was common among the troops in the trenches. Even in civil life it is by no means rare.

The chief **symptoms** in typical cases are a grayish, yellowish-gray, or yellowish-green membrane on the tonsils, pain on swallowing, a peculiarly offensive breath, and slight enlargement of the submaxillary or cervical lymph-nodes. The membrane is very friable and when detached leaves a bleeding surface. Ulceration frequently accompanies the membranous formation, and in severe cases there may be considerable destruction of tissue. The constitutional effects are, as a rule, much less than would be expected from the appearance of the throat, and in most cases consist merely of slight fever (99°–100° F.), headache and malaise. Occasionally, however, large areas of the throat and mouth are involved and the patient becomes acutely ill.

In the large majority of cases the prognosis is good, and under appropriate treatment recovery occurs within a week. Recrudescences and relapses, however, are not uncommon, and in exceptional cases necrosis spreads rapidly, great prostration ensues, and death occurs from exhaustion. Following deep ulceration there may be considerable scarring. The **diagnosis** is often suggested by the appearance of the throat and the slight constitutional disturbance but it can be made with certainty only by finding the specific organisms in smears made from the membrane. Other ulcero-membranous lesions, such as those of diphtheria, acute streptococcus sore throat, and syphilis, must be excluded.

**Treatment.**—Attention to the general health and to the hygiene of the mouth is always important. Locally, tincture of iodin, chromic acid (5 per cent.) or silver nitrate (5–10 per cent.) usually suffice, but arsenic, especially in the form of arsphenamin, is the most reliable remedy and should be used in all the more severe cases. Arsphenamin may be applied locally (5 to 10 per cent. solution in glycerin or water, twice daily) or, if necessary, administered intravenously. Campbell and Dyas[1] also speak favorably of Fowler's solution, swabbed on the affected parts three or four times a day. Pyorrhea, if present, must receive appropriate treatment, otherwise Vincent's infection is likely to persist.

## LUDWIG'S ANGINA

Ludwig's angina is an acute phlegmonous inflammation of the tissues beneath the jaw and about the floor of the mouth. It is usually due to streptococci, but other pyogenic organisms may be the exciting cause. It may occur as a complication of one of the specific infections, such as scarlatina, diphtheria or typhoid fever, or it may be secondary to ulceration of the mucous membrane of the mouth, suppurative tonsillitis, or a dento-alveolar abscess. A hard, painful swelling appears in the submaxillary triangle and rapidly spreads to the floor of the mouth and the tissues in front of the neck. Mastication, deglutition and articulation become difficult or impossible, and not rarely edema of the larynx supervenes causing intense dyspnea and sometimes suffocation. The constitutional symptoms are those of profound sepsis. Death frequently occurs within twenty-four or forty-eight hours. If the course is longer the inflammatory process may terminate in abscess and extensive sloughing. Fortunately, the disease is rare. Free incision below the jaw, exposing the submaxillary gland and extending through mylohyoid muscle, offers the only chance of recovery. It should be done at the earliest possible moment.

## RETROPHARYNGEAL ABSCESS

Retropharyngeal abscess is a suppurative inflammation of the lymph nodes in the posterior and lateral walls of the pharynx. It may be acute or chronic, the latter being rare and due to tuberculous or syphilitic caries of the upper cervical vertebræ. The acute form is observed chiefly in infancy, 90 per cent. of the cases occurring within the first three years of life. It may

[1] Jour. Amer. Med. Assoc., June 2, 1917.

develop as an apparently primary condition or it may follow one of the specific fevers, but in the large majority of cases it is a sequel to septic infection in the nose, accessory sinuses, throat or ears.

The most constant **symptoms** are difficulty in deglutition and a nasal intonation of the voice. Dyspnea also develops sooner or later, as a rule, and not infrequently it is accompanied by a slight croupy cough. Occasionally, the neck is rigid and the head is inclined to one side. A variable degree of fever is usually present. Sometimes inspection reveals bulging in the posterior pharyngeal wall, but unless a digital examination is made the abscess is very likely to be overlooked, as it is frequently too low in the pharynx to be seen through the mouth.

**Treatment** should be by incision, using for the purpose a bistoury guarded with adhesive plaster, and at the moment the abscess is opened elevating the infant's body somewhat above the level of its head so that the pus may run out of its mouth and not into its larynx. If not opened the abscess may cause asphyxia by directly compressing the larynx or by inducing laryngeal edema; or it may rupture spontaneously into the throat, and in this event the pus may enter the trachea and cause instant suffocation or set up a fatal bronchopneumonia. Occasionally, rupture occurs into the esophagus or, if the abscess is a chronic one, the pus burrows behind the esophagus to the posterior mediastinum. Rarely the abscess points externally in the anterior or in the posterior triangle of the neck. In a few instances fatal hemorrhage from erosion of the carotid artery has occurred (Bokai, Carmichael, Wylie and Wingrave, Travers).

## PTYALISM

An excessive secretion of saliva is most frequently a result of the too free use of certain drugs, especially mercury, iodids and pilocarpin; but it may also occur during pregnancy or menstruation, in chronic pancreatitis, in exophthalmic goitre, in rabies, and in certain nervous and mental diseases, particularly hysteria, epilepsy and mania. *Treatment* must be directed to the underlying condition. Atropin or tincture of belladonna often affords temporary relief.

## XEROSTOMIA

(Dry Mouth)

Persistent arrest of the secretion of the salivary and buccal glands may occur in diabetes, in hysteria, and after typhoid fever, mumps and other acute infections. In rare instances it seems to be a pure neurosis. It develops usually after the fortieth year and is much more common in females than in males. The tongue is dry, bare, red and fissured. Mastication, deglutition, and even articulation may be difficult. Dryness of the nose and eyes, rapid dental decay and swelling of the parotid glands sometimes accompany xerostomia. Digestion and general nutrition are usually unimpaired. No effective **treatment** is known. Faradism applied to the glands and pilocarpin ($\frac{1}{20}$ gr.–0.003 gm. on the tongue, three times a day) may be of some benefit for short periods. Bland oils, acacia, and glycerin sometimes afford temporary relief.

## PAROTITIS

(Mumps)

Inflammation of the parotid gland may be acute or chronic. Acute parotitis occurs as a specific infectious disease—mumps (see p. 256) and as a non-specific or symptomatic affection (parotid bubo).

**Acute symptomatic parotitis** may result from: (1) Infectious diseases, such as typhoid fever, pneumonia, bacillary dysentery, secondary syphilis, etc. It is probably most common in typhoid fever, but even in this disease it occurs in less than 1 per cent. of the cases. The gland may be infected by way of Stenson's duct or the blood stream.

(2) Operations on or injuries of the abdominal or pelvic organs, most frequently the genitalia. Infection is probably by way of Stenson's duct. Dryness of the mouth, stagnation of saliva, diminished mastication from enforced liquid diet, and injury to the gland or duct by the anesthetist have been suggested as predisposing factors in postoperative cases. Suppuration occurs in 50 per cent. of the cases.

(3) Diseases of the abdominal or pelvic organs, most frequently of the alimentary canal. Rolleston and Oliver[1] report that parotitis developed in 4.5 per cent. of 470 cases of peptic ulcer treated by exclusive rectal feeding, and that suppuration occurred in one-fourth of the cases.

(4) Chronic poisoning, as from iodids, mercury, and lead. Cases of iodic parotitis have been reported by Comby, Trautmann, Riesman, and others.

(5) Chronic diseases, after the occurrence of adynamia; for example, diabetes mellitus, chronic nephritis, and insanity.

(6) Intermittent Parotitis.—In this rare condition, of unknown etiology, the parotid gland periodically becomes swollen, painful and tender. Some cases seem to have been due to syphilis and others to chronic catarrh of the parotid ducts with the formation of fibrinous casts, or *sialodochitis fibrinosa*, examples of which have been reported by Emden, Kussmaul, Viaud[2] and others.

Other rare causes of acute parotitis are angio-neurotic edema (Talley), inflammation of the facial nerve (Gowers), hemiplegia (Gilbert and Villaret), acute erythema with purpura (Osler), x-ray applications to the face (Marquès) and pregnancy. Hawkins[3] cites the case of a woman, who developed parotitis during six successive pregnancies.

In the majority of cases the inflammation is unilateral. The affected gland is swollen, painful and tender. The constitutional symptoms are those of the primary disease. When the parotitis occurs in the course of a general infection there is a further elevation of temperature. Suppuration is common and if the abscess is allowed to go unrelieved, it may cause edema of the larynx, it may rupture through the skin, into the mouth, into the ear, or even into the cranial cavity, or it may burrow downward into the neck. The condition is a serious one and demands energetic treatment. In the early stages applications of ice, of lead-water and laudanum, of a saturated solution of magnesium sulphate, or of ichthyol ointment may afford relief. As soon as the presence of pus can be detected the gland should be incised.

**Chronic parotitis** is comparatively rare. It has been observed after mumps, following obstruction of the parotid duct by a salivary calculus, and in chronic metallic poisoning, chronic nephritis, syphilis, and tuberculosis.

[1] Brit. Med. Jour., 1909, vol. i, 1296.
[2] Thèse de Paris, 1894.
[3] Brit. Med. Jour., 1897, vol. i, 914.

It also occurs in *Mikulicz's*,[1] *syndrome*, which is characterized by a chronic symmetric and painless enlargement of the lacrimal and salivary glands, without any inflammatory reaction of the overlying skin. Iridocyclitis, sometimes resulting in blindness, has been observed in a number of cases (Bang).[2]

It is doubtful whether the condition is a definite pathologic entity. Some of the cases which have been reported under the name of Mikulicz's syndrome have apparently been examples of leukemia of the aleukemic type, Hodgkin's disease, tuberculosis of the salivary and lacrimal glands, or sialodochitis fibrinosa. A few cases of bilateral enlargement of the salivary glands occurring as a congenital and familial affection have been described (Leri,[3] Fontoynont.[4]

### TUMORS OF THE PAROTID GLAND

The so-called mixed tumors occur most frequently, but fibroma, adenoma, carcinoma, hemiangioma and lymphangioma have been described. Mixed tumors probably develop from abnormal inclusions of tissue during embryonal life and microscopically present in varying proportion epithelial elements, cartilage, fibrous tissue and mucous tissue. As a rule, they are firm, nodular, movable and painless, and show little tendency to involve the regional lymph-nodes. They usually grow very slowly and remain benign, although sarcomatous transformation occasionally ensues. Similar tumors occur in the submaxillary region, beneath the tongue, in the pharynx and in the upper lip.

## DISEASES OF THE ESOPHAGUS

### ESOPHAGITIS

**Acute esophagitis** may be due to the direct action of chemical, mechanical or thermic irritants, or it may arise as a secondary process in the course of infective diseases, such as diphtheria, scarlatina, smallpox, septicemia, etc. The lesions may be catarrhal, pseudomembranous, ulcerative, pustular, phlegmonous, or gangrenous. Corrosive substances frequently cause extensive sloughing and ulceration, which, in the event of recovery, result in stricture of the esophagus.

*Symptoms.*—In the milder forms the chief symptoms are pain upon swallowing and tenderness on pressure. Regurgitation of food may also occur as a result of esophageal spasm. In the severe forms swallowing is impossible, mucus, blood and pus are regurgitated, thirst is extreme, and weakness and emaciation soon develop.

*Treatment.*—In the mild cases treatment consists in restricting the diet to cool or lukewarm foods of a bland nature and in giving demulcent drinks, and, perhaps, bismuth subcarbonate suspended in water. In the more severe forms of the disease feeding by the mouth should be suspended and

[1] Münch. med. Woch., 1888, p. 759.
[2] Ugeskrift for Læger, 1918, lxxx, No. 15.
[3] Bull. et mém. Soc. méd. d. hôp. de Paris, 1912, xxxviii.
[4] Presse méd., Paris, 1911, xix.

nutrient enemas and enteroclysis with saline solution substituted. After a few days milk, cream and gelatin may be given by the mouth. After severe caustic burns it is advisable to use esophageal bougies, but in order that the ulcers may have time to heal, at least three weeks should be allowed to elapse before dilatation is begun.

**Chronic esophagitis** may follow acute esophagitis or result from continued irritation by alcohol, tobacco or pungent foods. The chief *symptoms* are a sense of burning or of pressure behind the sternum during deglutition and regurgitation of food and mucus. If the lesions are near the cardiac orifice cardio-spasm may ensue. *Treatment* consists in removing the cause and laving the esophagus with weak solutions of silver nitrate (1 per cent.) or argyrol (5 per cent.).

## SPASM OF THE ESOPHAGUS

(Esophagismus; Cardiospasm)

Spasm of the circular muscular fibers of the esophagus may be intermittent, occurring in definite attacks, with intervals of normal deglutition lasting weeks, months or years, or it may be more or less constant. The first form is observed chiefly in hysterical persons or in those of a distinctly neurotic temperament, and most frequently in young women, although occasionally it occurs in men. The attacks usually develop suddenly, being provoked, in many instances, by fright, anger, or some other form of emotional excitement. The contractions may occur at any point in the esophagus, but the pharyngeal orifice is, perhaps, most often affected.

The variability of the dysphagia is characteristic, the spasm being excited sometimes by one kind of food, sometimes by another. Occasionally, solids are swallowed more readily than liquids. The passage of an esophageal bougie may be temporarily inhibited, but if gentle pressure be used, the spasm soon relaxes, and then the instrument enters the stomach. Other stigmata of hysteria are frequently present, and as the attacks of dysphagia are usually of short duration and deglutition is normal in the intervals, emaciation is, as a rule, absent and secondary dilatation of the esophagus is not often seen.

Spasm of the esophagus occurring as a more or less constant condition usually affects the cardiac sphincter—*cardiospasm*. The cause of this affection is, as a rule, obscure. In some cases it is probably a reflex phenomenon excited by some morbid process above or below the diaphragm, such as pleuritic adhesions, etc., cholelithiasis, peptic ulcer, chronic appendicitis, etc., in other cases it is apparently the result of slight esophagitis, and in other cases still it is clearly a symptom of gross esophageal disease, such as carcinoma or ulcer. The average age of the patient at the onset of symptoms is about 30 or 35 years.

The onset may be gradual or sudden. The first symptom is often a sense of burning or of pressure at the end of the sternum or in the epigastrium at the moment the food is about to enter the stomach. In some cases pain occurs independently of deglutition and occasionally it is so severe as to be confused with biliary colic. Within a comparatively short time, if the condition persists, the esophageal wall undergoes hypertrophy, and then definite signs of stenosis supervene, the food lingering in the gullet and mouthfuls of it being returned. The dysphagia, unlike that due to cicatricial stricture of the esophagus or carcinoma, is not progressive and often is as pronounced with

liquids as with solids. Finally, the esophageal muscle yields under the increased strain and dilatation occurs. At this stage food is retained in the esophagus for several hours and large quantities are regurgitated from time to time, especially when the patient stoops or lies down. In some instances nocturnal regurgitation of food and mucus is the only obvious feature.

Occasionally the regurgitation is accompanied by dyspnea and cough. The x-ray, esophageal bougie and esophagoscope are valuable aids in diagnosis. As a rule, the x-ray should be used first so as to exclude thoracic aneurysm and gross malignant disease. Roentgenograms reveal a smooth blunt obstruction at the cardia, often with a diffuse symmetrical dilatation above it. An esophageal bougie meets with obstruction at a point about 40 or 45 cm. from the teeth, but under steady pressure this usually yields and then the instrument immediately enters the stomach. During moments of relaxation even a large bougie or a stomach tube may be introduced into the stomach without much difficulty. As seen through esophagoscope the cardia appears smooth and somewhat pale, rather than granular and injected, as in carcinoma.

The **prognosis** of cardiospasm is good when there is no serious underlying condition and appropriate treatment is instituted before the occurrence of marked esophageal dilatation.

**Treatment.**—In some cases relief is afforded by attention to the basic condition, if this can be found, by a soft, bland diet, proper hygiene, and the use of antispasmodics, especially belladonna and bromids. If these measures do not suffice good results may be expected from forcible dilatation of the cardiac sphincter by means of the hydrostatic dilator designed by Plummer, the instrument being guided by a previously swallowed silk thread. Of 246 patients treated by Plummer and Vinson,[1] 76 per cent. were completely cured, the majority by one dilatation, and 17 per cent. were definitely benefited.

## STENOSIS OF THE ESOPHAGUS

The term stenosis is applied to any narrowing of the lumen of the esophagus regardless of its character. The cause of stenosis may be extra-esophageal or intra-esophageal. Compression from without may be due to aortic aneurysm, mediastinal tumor or abscess, enlarged lymph-nodes, goiter, or pericardial effusion. The most important intra-esophageal conditions causing stenosis are stricture resulting from the cicatrization of ulcers, carcinoma, spasm of the esophagus, diverticula, and lodgment of foreign bodies.

**Symptoms.**—The chief symptoms of esophageal stenosis are gradually increasing difficulty in swallowing and regurgitation of food. The dysphagia is first experienced with solid foods and later with liquids. The regurgitation may take place immediately after eating or after the lapse of several hours, the time of its occurrence depending upon the site of the obstruction and the extent of the resultant esophageal dilatation. The returned food is soft and mixed with mucus, but its chemical reactions show that it has not reached the stomach. In all severe cases there is emaciation, the rapidity of its occurrence varying with the degree and character of the obstruction. The passage of esophageal bougies, radiographic examinations and esophagoscopy are invaluable means of determining not only the presence of stenosis, but also the exact position and degree of the obstruction.

[1] Med. Clin. of North Amer., Sept., 1921.

Before passing a bougie, the presence of aneurysm must always be excluded. In making the examination the patient should sit in front of a good light, with the head thrown slightly backward. The forefinger of the left hand should be used to depress the tongue, thus exposing the epiglottis, and to guide the tip of the bougie behind the larynx. The instrument, which has been previously smeared with olive oil, should be passed into the gullet steadily, but without undue force, as grave accidents may occur from the perforation of an ulcer or diverticulum. A slight resistance is normally encountered at the level of the cricoid cartilage, and to overcome this, it is advisable to have the patient bend his head forward and make an attempt to swallow. The use of cocain facilitates the passage of the bougie when the throat is very sensitive.

The determination of the nature of the stenosis is sometimes difficult. It requires a complete history of the case and a thorough physical examination.

## CARCINOMA OF THE ESOPHAGUS

Carcinoma of the esophagus constitutes 6 per cent. of all carcinomas and is, therefore, relatively uncommon. It is rarely seen in persons under 40 years of age and about three-fourths of the cases occur in men. The growth, which is usually of the squamous-cell variety, may be in any part of the esophagus. The cervical portion is less often attacked than any other part (10 per cent. of the cases), while the region of the bifurcation of the trachea is probably the most common site. Above the tumor there is some dilatation, although this is usually less marked than in other forms of stenosis.

**Symptoms.**—Dysphagia is usually the earliest and most obtrusive symptom. For a few weeks it may be intermittent, but soon it becomes permanent. At first only coarse food or large pieces of food are felt to stick in the gullet, but later the difficulty in swallowing extends to semi-solid food and sometimes even to liquids. As the stenosis progresses, regurgitation of food unmingled with gastric juice becomes an important feature, the time after eating of the food return varying with the location of the growth. With the occurrence of ulceration the regurgitated food may be streaked with blood or purulent material, and even fragments of the tumor itself may eventually be expelled. Pain is a variable symptom. Many patients experience merely a sense of pressure or of obstruction at some point behind the sternum during the act of deglutition. Others have actual pain from the time the food reaches the obstruction until it is regurgitated. In the later stages there is often persistent pain from extension of the disease to adjacent structures. As the obstruction becomes more complete hunger and thirst supervene, and the patient becomes exceedingly weak and emaciated.

Metastasis occurs somewhat less frequently than with carcinomas elsewhere, although when the lesion is in the lower third of the esophagus it is by no means rare in the liver. De Vries[1] observed it in this organ in 26 per cent. of 69 cases. Extension to adjacent structures is very common and is responsible for many symptoms not referable to the esophagus itself. Thus, involvement of the trachea or larynx may cause dyspnea and cough, of the recurrent laryngeal nerves, hoarseness or aphonia, of the sympathetic nerves, inequality of the pupils, etc. Invasion of the respiratory tract is commonly followed sooner or later by aspiration pneumonia or gangrene of the lung.

[1] Nederland. Tijd. v. Geneesk, 1919, No. 14.

Perforation into the mediastinum, into the larynx, trachea or a bronchus, into the pleura or pericardium, into the aorta or one of the other large blood-vessels may also occur.

The stomach-tube or esophageal bougie, the esophagoscope and the x-ray are valuable means of determining the actual existence of organic obstruction, as well as its exact position, degree, and nature. The stomach-tube is much safer than the bougie and should be used first. If any blood is withdrawn with the tube the bougie should not be used at all. Even the tube should not be passed until the presence of an aneurysm has been definitely excluded. An esophagoscopic examination shows clearly the state of the esophageal wall and affords a means of obtaining fragments of tissue for diagnostic purposes. It is especially useful in early cases. The x-ray is entirely free from danger and often gives important information as to conditions both inside and outside of the esophagus. Quite characteristic of carcinoma is a roentgenogram showing stenosis of the esophagus with moderate dilatation above it and a tortuous irregularity of the lumen.

**Diagnosis.**—This is based upon the patient's age, the previous history, and the results of a thorough physical examination, including roentgenography and esophagoscopy. It should be borne in mind that more than 80 per cent. of all persons who develop symptoms of esophageal obstruction after the age of 45 years suffer from malignant disease.

**Prognosis.**—Recovery is unknown. The duration is rarely more than two years and may be only a few months.

**Treatment.**—The diet should be limited to such nutritious foods as the patient is able to swallow. For a time concentrated broths, vegetable purées, soft boiled eggs, cream, milk, thin gruels, gelatin and custards are often taken without much difficulty. In selected cases the passage of a flexible, dilating bougie, once or twice a week, may be advisable. To lessen the risk of making false passages, or perforating the esophagus, a heavy silk thread which the patient has previously swallowed should be used to guide the instrument.[1] In some instances radium, applied by means of a bougie, has made the stricture temporarily more permeable. Resection of the esophagus has been attempted, but without good results, except in a few cases of cancer involving the cervical segment. When dilatation by the bougie is inadvisable or impossible, and an adequate supply of nourishment can no longer be taken by the mouth, gastrostomy is indicated. If the patient decides against the operation, recourse must be had to rectal feeding.

Gastrostomy prolongs life only for a short time, but it may make the patient more comfortable and, by permitting the inflammatory swelling about the growth to subside, may be followed by a temporary recovery of the power to swallow liquids and even soft food.

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## ULCERATION AND BENIGN STRICTURE OF THE ESOPHAGUS

Ulcer of the esophagus, other than that resulting from carcinoma, is comparatively rare. It may be due to (1) the action of corrosive poisons, such as lye, mineral acids, etc., (2) simple esophagitis, (3) foreign bodies, (4) the

[1] Plummer's whalebone bougie, provided with a series of perforated olive tips, is best for the purpose. With the aid of small sips of hot water the patient swallows about 6 yards of waxed silk, 3 yards during the evening and 3 yards the following morning. Eventually the thread passes through the structure and becomes anchored in the bowel. When made taut it serves as an accurate guide through the stricture. No food should be taken by the mouth for at least 6 hours previous to the instrumentation.

pressure of an aneurysm or tumor adjacent to the esophagus, (5) the decomposition of food in a diverticulum, (6) acute infections, such as typhoid fever diphtheria and scarlatina, (7) infectious granulomata, such as tuberculosis and syphilis, (8) lowered vitality from wasting diseases (cubital ulcers), or (9) the action of the gastric juice (peptic ulcers).

**Peptic ulcer** of the esophagus is very rare. It is situated, as a rule, near the lower end of the esophagus and is apparently caused by a reflux of gastric juice, permitted by insufficiency of the cardiac sphincter. Not infrequently, it involves the adjacent part of the stomach, and in some instances it is associated with ulcer of the pylorus or duodenum. The usual *symptoms* are pain, immediately after eating, at the xiphoid cartilage, radiating to the back between the shoulders; tenderness over the lower part of the sternum; dysphagia, the result of reflex esophageal spasm; vomiting, usually soon after meals; and hematemesis, frequently with melena. Perforation, usually fatal, is somewhat frequent, and occasionally it is the first sign of the ulcer. It may occur into the pleural cavity, pericardium, aorta, mediastinum, or lesser omental sac.

The *diagnosis* is often difficult. In a few instances it has been made with certainty by means of the esophagoscope. The two conditions most likely to cause confusion are ulcer of the stomach or duodenum and carcinoma of the esophagus. In gastric or duodenal ulcer there is no dysphagia and the pain occurs at a later period after eating. An insidious onset, progressive course, slight bleeding, cachexia, paralysis of the recurrent laryngeal nerve, etc. point to carcinoma, but an absolute diagnosis may be impossible without the aid of esophagoscopy and the microscopic examination of fragments of tissue removed from the lesion.

The *prognosis* is grave. Death frequently occurs from perforation or hemorrhage. Healing may result in stenosis. The *treatment* is that of gastric ulcer. Gastrostomy is indicated when there is recurrent hemorrhage or marked impairment of nutrition.

**Benign stricture of the esophagus** is usually caused by the healing of an ulcer produced by the swallowing of corrosive poisons, but it may follow the healing of ulcers due to peptic digestion, foreign bodies, typhoid fever or syphilis. The symptoms are gradually increasing dysphagia, regurgitation of food unmingled with gastric juice, and eventually, unless relief is obtained, marked emaciation and anemia. The esophageal bougie, x-ray, and esophagoscope are useful in determining the site and degree of obstruction, as well as its nature. The conditions most likely to be confused with benign stricture are compression of the esophagus from without by an aneurysm or a tumor, carcinoma of the esophagus, diverticulum of the esophagus, and esophagismus. In all cases the history of the patient is of great importance in the diagnosis.

**Treatment.**—Dilatation by means of bougies is, as a rule, necessary. After the swallowing of caustic substances it should be begun as soon as the ulcer has cicatrized, or, according to Lieblein,[1] in from 3 to 8 weeks. One thorough stretching may suffice, but in the larger majority of cases it is necessary to repeat the procedure at varying intervals during the life of the patient. When the stricture is impermeable to ordinary bougies, surgical measures are usually required. In some instances, however, it is possible to thread dilating bulbs over filiform bougies passed through the stricture with the aid of the esophagoscope. Occasionally, swallowing silver balls (Abercrombie) or lead shot (Socin) attached to strings is successful. Internal esophagotomy is rarely advisable, although it has occasionally given good

[1] Beitr. z. klin. Chir., 1908, lvi, 581.

results in strictures permeable to liquids but impermeable to instruments. When other measures fail gastrostomy is indicated. Retrograde catheterization through the gastric fistula may subsequently be tried, although after gastrostomy and complete rest of the esophagus it is the rule for impermeable strictures to become permeable from above.

## DIVERTICULA OF THE ESOPHAGUS

Diverticula are pouch-like dilatations of the esophagus. Two kinds are recognized: those due to traction and those due to pressure. The *traction diverticulum* is produced by the contraction of scar tissue arising from inflammation in some adjacent structure, usually a lymph-node, to which the esophagus has become adherent. It is most frequently situated at the level of the bifurcation of the trachea. It does not, as a rule, produce symptoms, because in the majority of cases it is small and the mouth of the pouch is at a lower level than the apex. The *pressure or pulsion diverticulum* is really a hernia of the mucosa through the muscularis. It is produced by the pressure of boluses of food upon an area of the esophageal wall that is congenitally weak or imperfect. The usual site is the posterior or postero-lateral aspect of the esophagus at its junction with the pharynx. The sac, which commonly passes downward to the left, may be of considerable size and extend well into the thorax.

**Symptoms.**—The symptoms do not usually manifest themselves until middle life. The earliest indications are uncomfortable sensations in the throat, increased flow of saliva, and frequent expectoration of mucus. After a time there is difficulty in swallowing and a regurgitation of undigested food at varying periods, even to a day or two after eating. A distinct swelling may appear on the side of the neck and pressure in this situation may empty the contents of the pouch into the pharynx or result in the gurgling up of gas. Peculiar sounds are sometimes produced when food is taken, and not rarely there is great fetor of the breath from decomposition of the contents of a diverticulum. A large sac when distended may cause cough, hoarseness and dyspnea from pressure. The diagnosis is best made by the x-ray after a barium or bismuth meal. The roentgenogram usually shows a symmetrical sac with a smooth rounded base.

A diverticulum may exist for years without causing very serious disturbances, but in many cases the symptoms gradually grow worse and eventually death occurs from inanition, abscess, or septic pneumonia. Occasionally carcinoma has developed as a result of the local irritation.

**Treatment.**—Palliative treatment consists in frequent irrigation of the sac, and, if necessary, feeding by the tube. Sometimes the patient is able to find a certain position while eating which greatly lessens the difficulty in deglutition. In the case of small diverticula the passage of large sounds occasionally affords considerable relief. The only curative treatment consists in removing the sac or in obliterating it by a method of infolding, and, at present, these procedures are feasible only when the diverticulum is situated in the neck. Judd[1] reports 35 operative cases with 2 deaths (5.7 per cent.) and almost complete relief in the other 33.

[1] Surg., Gynec. and Obstet., 1918, xxvii.

# DISEASES OF THE STOMACH

## DISORDERS OF THE GASTRIC FUNCTIONS

The stomach is an important organ for the preparation of food for intestinal digestion. It is, however, not essential to life. Its chief functions are motor; through these the gastric contents are thoroughly mixed and finally discharged into the duodenum. The chemical functions of the stomach are of secondary importance, the small intestine being capable alone of maintaining the entire work of digestion. Absorption from the stomach, so far as water and the products of digestion are concerned, is almost nil. The investigations of Gaskell, Langley, Lennander, James Mackenzie and others have demonstrated conclusively that the stomach in common with other viscera is not sensitive to tactile or painful stimulation, and that pain and other uncomfortable sensations which appear to be located in the viscus really have their seat in one or other of the structures of the abdominal wall, the afferent sympathetic nerves conveying certain stimuli originating in the stomach to the segments of the spinal cord from which emanate the sensory nerves supplying the skin and muscles in the area of pain or discomfort. The nature of the stimuli which are thus translated into sensation is not definitely known, but it is supposed that increased tension in the wall of the stomach, such as may result from irregular or excessive contraction of the muscular coat, is a factor.

Disturbances of the functions of the stomach are extremely common and occur in the most diverse disorders. In a certain proportion of cases they are the direct result of a definite anatomic lesion of the stomach itself, as catarrh, ulcer, cancer, etc. In many cases they are manifestations of disease in some other organ, either adjacent to or remote from the stomach, such as the liver, bowel, pancreas, lungs, heart, brain, etc., or of some constitutional condition, such as anemia, diabetes, hyperthyroidism, etc. Not infrequently in these cases the primary disease is so overshadowed by the gastric disturbance that it fails of recognition. In this connection reference may be made to the hypersecretion or hyposecretion, with its accompanying symptoms, so frequently observed in chronic disease of the appendix or gall-bladder; to the persistent nausea and vomiting of pregnancy, chlorosis, uremia, pulmonary tuberculosis and brain tumor; to the painful crises of tabes dorsalis and sclerosis of the abdominal vessels; and to the multiplicity of distressing symptoms involving the stomach (nervous dyspepsia) sometimes occurring in neurasthenia and hysteria. Finally, there is a group of cases (a comparatively small one) in which the gastric disturbance appears to be purely functional and to rest on no other basis than some derangement of the gastric nervous mechanism itself.

Functional disturbances of the stomach may occur singly or in combination. Various combinations with one another and also with organic disease are observed. Thus, in one case there may be impairment of motility with hyposecretion, in another hypersecretion, hypermotility and periodic pylorospasm, and in another hypersecretion, pylorospasm, and peptic ulcer. It must be noted also that derangements which are primarily functional may eventually give rise to others which are definitely organic. Thus, simple atony may finally result in dilatation of the stomach, and it is possible that hypersecretion with pylorospasm may sometimes lead to erosion and ultimately to actual ulceration.

**The Appetite.**—Appetite, or relish for food, depends only in part upon the condition of the stomach. It is not precisely synonymous with hunger, although the two conditions are closely correlated. *Anorexia*, or lack of

appetite, acompanies many diseases of the stomach, as well as a great variety of disorders in which the stomach is not directly involved, for example, acute infections, anemic states, tuberculosis and other wasting diseases. As a purely nervous phenomenon it sometimes occurs in hysteria, in neurasthenia and in certain psychoses, and occasionally it appears in healthy subjects after some violent psychic shock or depressing emotion.

*Bulimia* (hyperorexia) is abnormal increase in the sensation of hunger. It is common during convalescence from acute disease; it is sometimes observed in helminthiasis, in diabetes, in hysteria, in certain psychoses, in hyperthyroidism, and in tumors of the brain. It is occasionally seen in diseases of the stomach, especially in those forms in which both secretion and motility are exaggerated. It rarely occurs as an independent neurosis. Bulimia differs somewhat from *polyphagia*. Patients with the former, although irresistibly hungry, are often satisfied if they eat small meals, while patients with the latter are only satisfied if they eat large quantities of food. *Akoria* is an entire lack of the sensation of satiation. It may exist without any increase in the desire for food. *Parorexia* is a qualitative perversion of appetite. If it consists in a craving for articles that are not foods, such as chalk or earth, it is known as *pica*. Parorexia is sometimes noted in pregnancy, in chlorosis, in helminthiasis, in hysteria and in certain psychoses.

**Disturbances of the Motor Functions.**—The rate at which the stomach empties itself depends upon the condition of the pylorus, the strength of peristalsis and to some extent upon the tone of the gastric muscle. In health the state of pyloric sphincter depends largely upon the reaction of the duodenal contents, the pylorus closing after each discharge of acid chyme into the duodenum and relaxing again as soon as the chyme has been neutralized by the alkali of the pancreatic, hepatic, and intestinal secretions. Thus, closure and relaxation successively follow each other until the stomach is completely emptied, the whole process requiring from 3 to 7 hours, according to the amount and character of the food.

Peristaltic movements are the wave-like contractions by which the food is thoroughly mixed with the gastric secretions and propelled onward into the intestines. By tonicity is meant the state of tension in the gastric muscle, or the property that enables the stomach to exert the requisite degree of pressure upon its contents. *Hypermotility* of the stomach is an acceleration of gastric peristalsis with abnormally rapid propulsion of the chyme into the bowel. It may occur as a primary neurosis (peristaltic unrest), but much more frequently it is a result of achylia, diarrheal conditions, non-obstructive duodenal ulcer, or gastric cancer with achylia and a gaping pylorus. Uncomplicated hypermotility does not usually cause any serious disturbance, but when it is associated with pyloric stenosis the patient may experience a disagreeable sensation and the movements of the stomach may even be visible through the abdominal wall. *Hypomotility* with delayed emptying of the stomach may depend upon atony of the stomach, gastrectasis, or obstruction at or near the pylorus. The obstruction may be due to carcinoma, stricture, adhesions, obstructing ulcer, or persistent pylorospasm from cholecystitis, appendicitis, etc. The emptying time of the stomach may be determined either by the stomach tube or the x-ray. Normally, when the stomach is washed out seven hours after the Riegel test-meal, consisting of meat broth (400 mils), beef-steak (150 grams), mashed potatoes (50 grams) and a roll, or seven hours after the Cohnheim meal, consisting of a plate of porridge cooked with raisins, and one or two slices of bread, it is found empty. After a meal consisting of cereal gruel (300–500 grams) and barium sulphate (100–120 grams) the average emptying time in health, as shown

as by x-ray, is from 3 to 5 hours. Large residues 6 hours or longer after the barium meal or 12 hours after the Riegel or Cohnheim meal almost always indicate mechanical obstruction at or near the outlet of the stomach.

*Excessive hypertonicity* of the stomach (gastrospasm) is best detected by the roentgen ray. It may be diffuse or regional. In the diffuse form the stomach is contracted and uniformly tense and immobile. Regional gastrospasm may affect the body of the stomach producing a more or less deep indentation (incisura) or an intermediate constriction with biloculation (spasmodic hour-glass stomach); or it may, involve the sphincters of the organ, causing in one case pylorospasm and in the other cardiospasm. In general, gastrospasm may occur (1) as a primary neurosis, due to abnormal irritability of the vagi (vagatony) or to exaggerated sensitiveness of the stomach to hydrochloric acid (so-called hyperchlorhydria); it may be caused (2) by a lesion within the stomach, especially gastric ulcer; or it may be induced (3) by a lesion outside of the stomach, such as duodenal ulcer, disease of the gallbladder or appendix, renal calculus, tabes, etc. The symptoms of cardiospasm and of spasmodic hour-glass-stomach are described on pages 405 and 433 respectively. Pylorospasm is frequently manifested by cramp-like epigastric pain coming on suddenly at the height of digestion and sometimes radiating along the costal border to the back. Vomiting or acid regurgitation may also occur and not rarely the pain is accompanied by a tender point just to the right of the median line and about 3 or 4 centimeters above the umbilicus. It is characteristic of gastrospasm that it disappears under general anesthesia and usually after the administration of belladonna or atropin in full doses. It is, as a rule, intermittent, but when due to ulcer or cancer it may be almost continuous. Frequently recurring or persistent pylorospasm commonly results in atony and ectasia. The treatment of gastrospasm is that of the underlying condition.

A condition sometimes observed in air-swallowers apparently as the result of simultaneous spasm of the cardia and pylorus is *pneumatosis*. It is characterized by painful distention of the stomach with, at times, severe nervous symptoms. It is usually induced by emotional excitement or mental strain and is relieved at once by the introduction of a stomach-tube.

Another condition which is due in part to aërophagia and in part to forcible clonic contractions of the stomach is *nervous belching* (eructatio nervosa). This is observed chiefly in neuropathic subjects and is characterized by paroxysmal attacks of noisy belching, sometimes persisting for hours or even days. The attacks are usually brought on by some psychic disturbance and bear no definite relation to the quality or quantity of the food or to the time of eating. Some patients can induce them by an effort of the will. The gas unlike that produced by fermentation has no unpleasant odor. Treatment must be directed mainly to the underlying condition. When the attacks come on the patient should be instructed to keep his mouth open, for by so doing the swallowing of more air is made impossible.

*Vomiting*, or the more or less forcible expulsion of the contents of the stomach through the mouth, is brought about by a convulsive contraction of the abdominal muscles, aided by contraction of the walls of the stomach itself, while the pylorus is tightly closed and the cardiac sphincter is relaxed. This complex mechanism is apparently under the control of a special center located in the medulla. Vomiting may be induced by causes which affect directly the vomiting center, such as intracranial disease, certain drugs (apomorphin) and certain endogenous or exogenous poisons, or it may occur as a reflex phenomenon excited by irritation of various afferent nerves, particularly those of the stomach, but also those of other organs and struc-

tures. Vomiting resulting from intracranial disease ("cerebral vomiting"), such as meningitis or tumor, is often independent of food, unaccompanied by nausea, free from effort, of the projectile type, and associated with persistent headache, which it does not relieve. Vomiting occurring periodically, at irregular intervals and without relation to the quantity or quality of the food eaten should in adults excite a suspicion of tabetic crises. The periodic or cyclic vomiting occurring in early childhood, and which occasionally proves fatal, is of obscure origin. It is characterized by marked prostration and not rarely by the presence of $\beta$-oxybutyric acid in the urine. It has been ascribed to an intoxication arising from disordered metabolism (Griffith), to acidosis (Edsall), to intermittent hypersecretion (Snow) and to infantile migraine (Rachford). Autopsy has occasionally revealed obstruction at the pylorus or duodenum (Russell, Gordon).

Vomiting after paroxysmal cough is not peculiar to any disease, but in children it is seen especially in pertussis and in adults in pulmonary tuberculosis and decompensated cardiac disease. In primary lesions of the stomach vomiting usually occurs some time after eating, except in acute gastritis, when it occurs soon after a meal.

Recurrent vomiting of large quantities of food, some of which has been retained much longer than the usual time, points strongly to obstructive gastrectasis. The vomiting of material having the odor and color of feces (fecal vomiting) is a characteristic sign of obstruction in the lower part of small intestine or in the colon.

*Hypotonicity of the gastric muscle* is usually referred to as atony of the stomach. Atony of the milder type may have little effect upon the emptying power of the stomach if the gastric peristalsis remains fairly active. In pronounced cases, however, there is always a tendency for some particles of food to remain longer than the normal time in the dependent part of the relaxed organ. Residues after twelve hours never occur with simple atony, but signify dilatation of the stomach and nearly always pyloric stenosis.

*Insufficiency of the cardiac sphincter* is closely related to habitual regurgitation and to rumination or merycism. In regurgitation food rises from the stomach into the throat and is then expectorated or swallowed again. In *rumination* the food is brought up as in regurgitation, but instead of being immediately expectorated or reswallowed, it is subjected to a second mastication, the patient deriving a certain amount of pleasure or satisfaction from the act. Rumination is observed chiefly in neuropathic subjects. In some cases it is hereditary or acquired by imitation. An intermittent form is occasionally a manifestation of epilepsy.

*Insufficiency of the pylorus* is said to exist when the pyloric sphincter is incapable of preventing during digestion the too rapid escape of the ingesta from the stomach into the bowel. It is rarely observed as a primary functional condition, but usually it is a result of some organic disease of the stomach, such as carcinoma, which has converted the pylorus into an inelastic tube or has stretched it to an abnormal degree. The condition permits a reflux of bile and duodenal contents into the stomach and is sometimes the cause of lienteric diarrhea. It is best detected by the x-ray. Hypomotility from atony of the gastric muscle and weak peristalsis may fail to cause food retention if its tendency in this direction is offset by pyloric insufficiency.

**Disturbances of Secretion.**—The gastric secretion varies considerably both in quantity and in degree of acidity. *Hypersecretion* may be transitory, it may occur periodically, or it may be persistent without intermissions. It may occur only during the course of digestion or it may continue even in the fasting stomach. With increased secretion the acid is usually high, but

it may be that of the average person or lower. The percentage of hydrochloric acid in the pure gastric juice probably never exceeds the maximum that may be found in health (0.5 per cent.), but many pathologic conditions are associated with low acid figures and even with anacidity. The percentage of hydrochloric acid in the mixture of gastric juice and food that is subjected to ordinary analysis may approach that of pure gastric secretion, but it never exceeds it and probably in no pathologic condition is the degree of hydrochloric acidity higher than may sometimes be found in perfectly normal individuals. Rehfuss and others have shown that an acidity of 100 or over (0.36 per cent.) is frequently observed normally and is not to be construed as hyperacidity. So-called "hyperchlorhydria"—post-prandial epigastric pain, which is relieved by bland food, alkalies, vomiting or lavage—apparently signifies merely lessened tolerance for acid, as the same syndrome is not uncommonly observed with average acidity or even with low acidity. The causes of *hypersecretion* and *high acidity* are considered on page 418.

The secretion of pepsin is not necessarily parallel with that of hydrochloric acid, nevertheless when the secretion of acid is very low that of pepsin is usually also low. The term achylia gastrica was employed first by Einhorn to designate an absence of both free hydrochloric acid and pepsin, but as used at present it signifies a complete absence of free acid and low total acidity.

*Hypochlorhydria* or true *achylia gastrica* is present in many cases of chronic gastritis and gastric carcinoma, as well as in degeneration of the gastric mucosa secondary to tuberculosis and other wasting diseases. It is not infrequently observed in certain diseases not directly affecting the stomach, such as advanced carcinoma of other organs, pernicious anemia and other severe anemias, advanced cardio-vascular disease, chronic cholecystitis, hyperthyroidism, gout and diabetes. Finally, it may occur as a simple functional disturbance, arising from depression of the secretory nerves (vagi).

It is very important to distinguish between true achylia and spurious achylia, and this can be done most satisfactorily by the fractional method of gastric analysis. This consists in withdrawing and examining small samples of the gastric contents at frequent intervals during the whole cycle of gastric digestion, using for the purpose the small Rehfuss tube which may be left in the stomach for a considerable time without much discomfort to the patient. In *true achylia* acid is absent throughout the entire process of digestion. In *spurious achylia* gastric secretion is merely delayed, and while no free acid may be present during the first hour, an abundance may be found after this period. Although hydrochloric acid is an important factor in promoting pancreatic secretion, achylia does not necessarily cause unpleasant symptoms or serious disturbances of nutrition, if the motility of the stomach continues normal and the functions of the intestines remain intact. It is probable that in the absence of hydrochloric acid some other agent in the duodenal contents may serve to stimulate pancreatic secretion. In some cases of achylia there is complaint of local discomfort after eating, with eructations and occasional vomiting of undigested food. In other cases (about 40 per cent.) there is refractory diarrhea which has been variously ascribed to the rapid discharge of insufficiently digested food into the bowel, to exaggerated intestinal peristalsis, to secondary inflammation of the intestine, and to disturbance of the pancreatic functions.

Although many patients with so-called primary achylia remain in good health for years, actual cure is usually difficult and in some instances apparently unattainable. Treatment should be directed chiefly toward main-

taining intestinal digestion at as high a degree of efficiency as possible. A mixed diet is usually permissible, but all food should be nutritious, well-cooked, finely divided, soft and easily digestible. Vegetables rich in cellulose should be avoided. Fat in the form of butter and cream is, as a rule, well borne. Hydrochloric acid is indicated and in some cases it acts well. Not rarely, however, an alkali (sodium bicarbonate or bismuth subcarbonate) with pancreatin proves more effective. Bitters before meals may be of service. Measures to improve the patient's general condition often produce better results than any treatment directed especially to the stomach.

**Disturbances of Sensation Referred to the Stomach.**—A variety of abnormal sensations—pressure, fulness, burning, neuralgic pain, etc.—are referred to the stomach. In some cases these appear only after eating; in other cases they occur independently of the ingestion of food. The immediate cause of abnormal sensations arising from the stomach is supposed to be increased tension or cramp of the muscular coat of the organ, while their actual seat is probably the abdominal wall, the stomach itself being insensitive to painful stimulation. Neuralgic pain of gastric origin is known as *gastralgia*. This may be secondary to some other condition directly involving the stomach, such as ulcer, cancer, or perigastric adhesions; it may be caused by reflexes from other organs, as the gall bladder, appendix, ovary kidney, etc.; it may constitute a part of the gastric crisis of locomotor ataxia; it may be associated with some constitutional disturbance, such as gout, chlorosis, or hyperthyroidism; and, finally, in very rare instances, it may occur as an independent neurosis.

True nervous gastralgia is characterized by paroxysms of severe pain in the epigastrium, occurring suddenly at irregular intervals and lasting from a few minutes to several hours. The attacks bear no relation to eating and may appear at any time of the day or night. The pain often radiates to the chest and back and may be so intense as to cause weakness and pallor. Firm pressure over the stomach may afford relief and so may the taking of food. Vomiting is rare, and the functions of the stomach are, as a rule, well performed. Other nervous symptoms are frequently present. Care must be taken to exclude peptic ulcer, gastric cancer, hyperchlorhydria, perigastric adhesions, chronic appendicitis, intestinal hernia, cholelithias, renal colic, lead colic, pressure myelitis, intercostal neuralgia, crises of tabes, angina pectoris, aneurysm of the abdominal aorta, and angina abdominis. The best drugs for combating the attacks are chloroform 3 to 5 minims (0.2–0.3 mils), aromatic spirit of ammonia, ½ fluidram (2.0 mils), brandy, 1 to 2 fluidrams (4.0–8.0 mils), and antipyrin, 5 to 8 grains (0.3–0.5 gm.). Hot applications are useful. The treatment in the interval is that of nervous dyspepsia (see p. 417).

**Nervous Dyspepsia.**—This name is applied to a syndrome made up of various gastric neuroses, in which, however, sensory disturbances are always the most conspicuous. The condition usually occurs in those of a distinctly nervous temperament and mental overexertion, worry, sexual excesses, and abuse of alcohol or tobacco are potent etiologic factors. It is frequently associated with neurasthenia. In some cases it is excited by reflex irritation from other organs, as the eyes or genitalia. It is also observed at times in chlorosis, hyperthyroidism and other general diseases.

*Symptoms.*—Epigastric distress during the period of digestion is the most prominent symptom. It varies in degree from a feeling of discomfort to intense pain (gastralgia). There is rarely tenderness, but the skin over the stomach is often abnormally sensitive. The appetite is very variable—at one time it may be normal, at another time lost, and at another time inordi-

nate. Occasionally there is parorexia. Belching occurs in many cases, but vomiting is uncommon. Exaggerated peristaltic movements, attended with gurgling noises, are often perceptible to the patient. Other nervous symptoms, such as headache, dizziness, disturbed sleep, lassitude, palpitation, abdominal pulsation, tenderness along the spine, etc., are usually in evidence. The degree of gastric acidity is, as a rule, about the average of that in health, but it may be low or high. In the majority of cases the motility of the stomach is not affected, the viscus emptying itself within the normal time. The symptoms are usually confined to the period of digestion; they are disproportionate to any anomalies of gastric secretion or motility; they vary greatly from day to day, according to the mood of the patient; they are not materially influenced by the quality or quantity of the food, and they are not, as a rule, accompanied by any decided impairment of the general nutrition. It must be borne in mind that nervous dyspepsia as a primary neurosis is uncommon, and that in the vast majority of cases the syndrome is due to a lesion of the stomach itself, to other abdominal disease, or to some constitutional disturbance.

*Treatment.*—The treatment is chiefly that of neurasthenia. In patients who are mentally tired, systematic exercise in the open air, hydrotherapy, etc. often prove beneficial. A change of scene may effect a cure. On the other hand, the physically exhausted and anemic may require the "rest-cure." The diet should consist of nutritious but readily digestible food. Tonics, especially nux vomica, iron and arsenic, are often indicated. Short courses of bromids may be of value. Such remedies as asafetida, sumbul and valerian are sometimes useful.

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## HYPERCHLORHYDRIA AND GASTRIC HYPERSECRETION

The concentration of hydrochloric acid in freshly secreted gastric juice unmixed with food ("native" juice) is remarkably constant and amounts to 0.35 to 0.5 per cent. This concentration is rapidly reduced to the optimum level of 0.15 to 0.2 per cent. through the neutralizing effects of gastric mucus and alkaline fluid entering the stomach from the duodenum. The percentage of acid in pure gastric juice may be reduced in disease, but the evidence is lacking that it can be materially increased under any pathologic condition. The percentage of acid in the mixture of juice and food which is subjected to clinical analysis may approach that of the pure gastric juice of normal persons, but it never exceeds it. What is usually designated as "hyperacidity" probably depends mainly upon excessive secretion of gastric juice, upon deficient gastric motility with retarded emptying of the stomach, or upon delay in the entrance of the alkaline intestinal secretions into the stomach. The total titratable acidity of the gastric contents has been considered to be normally about 50 to 80 degrees[1] (0.2 to 0.28 per cent. HCl), but these figures are founded on the single tube test, which indicates only one phase of the digestive cycle. Employing the fractional method of gastric analysis which follows the entire cycle of digestion, Rehfuss and others have recently shown that a total acidity of 100° or over (0.36 per cent. HCl) is not

[1] Clinically, the amount of acidity is usually expressed by the number of mils of tenth-normal sodium hydroxid solution which are required to neutralize 100 mils of gastric juice, each mils representing one *degree* of acidity. Thus, if 5 mils of the hydroxid solution were required to neutralize 10 mils of gastric juice, the degree of acidity would be 50. Each degree of acidity is equivalent to 0.00365 per cent. of HCl, and, therefore, 50° would represent 0.182 *per cent.* (50 × 0.00365) of HCl.

rarely encountered in normal persons and that *pathologically there is no range of titratable acidity that cannot be found under certain conditions in health.* Higher acidities occur with protein foods than with cereals, and therefore high figures with the simple Ewald meal are especially significant. The total acidity of the gastric contents fairly represents the hydrochloric acid value, provided there is no decided amount of organic acid present.

The normal fasting stomach usually contains from 10 to 50 mils of clear or slightly cloudy secretion, containing, as a rule, traces of bile and saliva, and showing an average total acidity of 30 and a free acidity of 18. Food residue is never present unless there is delayed motility. Amounts of fasting contents in excess 50 mils usually indicate abnormal secretory activity or impaired motility. Findings of 80, 100, or even 150 mils are not uncommon. The acidity in the majority of cases of hypersecretion is high, but it may be that of the average normal person or lower. Hypersecretion may occur only on the taking of food (*alimentary hypersecretion*), but in many instances it persists during the fasting state (*continuous hypersecretion*). Fasting hypersecretion may continue without intermissions or it may occur periodically. The persistent type is known as *Reichmann's disease.*[1]

**Etiology.**—High gastric acidity, so-called hyperchlorhydria, is a frequent accompaniment of certain organic diseases of the stomach, especially peptic ulcer and acid gastritis. In many instances it depends upon reflex irritation originating in some lesion outside of the stomach, notably chronic appendicitis, chronic cholecystitis, or abdominal adhesions. It is sometimes observed in the crisis of tabes dorsalis and it is not uncommon in chlorosis. Finally, it may occur as a secretory neurosis, independently of any other disease. Hypersecretion depends upon increased irritability of the gastric mucosa or the secretory nerves of the stomach and occurs under the same etiologic conditions as so-called hyperacidity with which it is frequently associated.

Examples of "hyperchlorhydria" or the digestive form of hypersecretion of purely nervous origin are sometimes observed in young adults engaged in clerical or professional work. Mechanics and laborers furnish but a small percentage of cases. Indiscretions in eating or drinking, the excessive use of tobacco or alcohol, and, above all, mental or emotional strain are important causes. Continuous interdigestive or fasting hypersecretion, especially if pronounced, is always strongly suggestive of peptic ulcer. The intermittent form of continuous or interdigestive hypersecretion sometimes occurs in brain tumor, migraine, tabes dorsalis and neurotic instability with vagotonia.

**Symptoms.**—In many cases of digestive hyperacidity there is epigastric discomfort or actual burning pain, which comes on from half an hour to two or three hours after eating and which is relieved by alkalies, bland food or evacuation of the stomach. In continuous hypersecretion pain is often experienced also at times when the stomach should be empty, as during the night. In any case the pain is more readily induced by starchy foods than by protein foods. Less constant symptoms are acid eructations, headache and vomiting of sour material at the height of the pain. It is noteworthy, however, that these symptoms of hyperchlorhydria may occur with normal or even subnormal gastric acidity, and on the other hand, that a great excess of free acid may be present without any symptoms at all (larval hyperchlorhydria). Moreover, it has been shown that the introduction of hydrochloric acid into the stomach in amounts much in excess of those found in disease is not productive of pain, and it is well known that the hyperchlorhydric syndrome often disappears under appropriate treatment even though the degree of acidity still remains high. It is obvious, therefore, that an

[1] Berlin. klin. Woch., 1882, 1884, 1887.

excess of acid is not the sole factor in producing the symptoms. It is likely that the subjective hyperchlorhydric syndrome is the peripheral expression of a cramp or spasm affecting the gastric musculature, which may occur even with moderate or low acidity if the nerves or nerve-centers are sufficiently irritable.

**Diagnosis.**—An exact diagnosis of hyperchlorhydria, if we mean by this term an actual increase of the hydrochloric acidity of the stomach rather than an intolerance of the stomach to hydrochloric acid, can be made only by examination of the gastric contents. It is necessary to add, however, that the findings in a single tube test one hour after a test breakfast are often misleading and that reliable information can be obtained only by the fractional method which follows the entire cycle of digestion. The diagnosis of continuous hypersecretion is made by the finding of considerable amounts of gastric juice, unmixed with food remnants, in the stomach early in the morning before breakfast. In deciding whether hyperchlorhydria or hypersecretion is a primary or secondary phenomenon the history of the case, the course of the disease, and all the symptoms presented must be carefully considered.

**Prognosis.**—In uncomplicated cases the prognosis, as regards freedom from discomfort, is good, if the cause can be removed. Relapses, however, are common.

**Treatment.**—The chief indications are to remove the underlying cause of the condition, to lessen the morbid impressionability of the nervous system, and to prevent any direct irritation of the stomach. Regular meals, regulation of the temperature of the food and drink, thorough mastication, avoidance of excesses in eating, drinking, and smoking are cardinal points. Thorough mastication is especially important, for the more comminuted the food, the more bland it is, the more acid it binds, and the shorter its stay in the stomach. Although the patient is temporarily more comfortable upon protein foods experience has shown that the best diet is a liberal mixed one of nutritious, bland, easily digestible food. Foods to which vinegar and spices have been added and highly seasoned dishes of all kinds must be interdicted. Fats in the form of butter, cream and olive oil usually prove acceptable and efficacious. They not only depress acid secretion (Boas, Pawlow, Bachmann and others) but they also cause an actual reduction of acidity by inviting a regurgitation of the alkaline duodenal contents into the stomach. Tea and coffee should be used sparingly, if at all. Alcohol is usually inadmissible. Water-drinking at meals, provided it is not excessive and the temperature of the water is not too low, is not objectionable. Excessive smoking is distinctly harmful.

Alkalies in the form of sodium bicarbonate, magnesia or chalk, administered at the height of digestion, almost invariably afford temporary relief. For securing more permanent effects bismuth subcarbonate in doses of 20 grains (1.3 gm.) or more or silver nitrate in doses of $\frac{1}{6}$–$\frac{1}{2}$ grain (0.01–0.03 gm.), with extract of hyoscyamus or belladonna, half an hour before meals is often useful. Sedatives, such as the bromids, are sometimes of service. In hyperchlorhydria the result of brain tire, travel, properly directed, often accomplishes much more than any form of medicinal or dietetic treatment, and may be confidently recommended to those who can afford it.

## ATONY OF THE STOMACH

(Myasthenia Gastrica)

**Definition.**—Atony of the stomach consists in relaxation of the muscular coat of the stomach and slight insufficiency of its propulsive power. As the stomach does not contract upon its contents as firmly as it should there is a tendency for remnants of food to remain abnormally long in the most dependent portion of the organ. Complete evacuation eventually occurs, but stagnation and gastrectasis may supervene if the condition is long continued.

**Etiology.**—Atony of the stomach is common. It is often a part of a general myasthenia produced by overwork, insufficient or unsuitable food, insanitary environment, or chronic disease, such as anemia, tuberculosis, etc.; it may follow acute infections; it may depend solely upon dietetic errors, especially overloading of the stomach or insufficient mastication; it may be an accompaniment or sequel of some other disease of the stomach, such as chronic gastritis, gastric cancer, or gastroptosis; it may be a concomitant of chronic appendicitis or cholecystitis, or other abdominal disease.

**Symptoms.**—In simple atony of the stomach the chief symptoms are a sense of fulness or discomfort in the epigastrium after meals, especially if the latter have been bulky, and frequent belching of gas. The succussion splash is often present several hours after eating. The severity of the symptoms usually bears a definite relation to the quantity of food taken. Fluids are as likely to cause discomfort as solids. As a rule, there is neither vomiting nor actual pain. The appetite is often good, the general health is not seriously affected and the symptoms entirely subside upon evacuation of the stomach. An exact diagnosis is made by determining the emptying time of the stomach by the stomach tube or the roentgen-ray. No remnants of food are found in the fasting stomach in the morning, but a variable amount of solid residue is obtained by means of the stomach-tube seven hours after a Riegel test-meal (see p. 412) or is seen in the stomach by x-ray six hours after a barium meal. The size, position, and contour of the stomach, as shown by the roentgen-ray is, normal. The degree of motor insufficiency may be estimated by the amount of residue remaining in the viscus at the times mentioned.

**Prognosis.**—The outlook is good if the cause is removable.

**Treatment.**—The first indication is to eliminate the causal factor. The food should be readily digestible, small in bulk, finely divided and nutritious. Fluids, except in moderate quantities, and coarse vegetables are to be avoided. The diet may include tender meats, eggs, oysters, boiled fish, well-cooked cereals, steamed rice, purée of potato, spinach or peas, stale bread and fresh butter. It is rarely necessary to increase the number of meals. Rest for at least an hour after large meals is to be recommended. Exercise in the open air and frequent bathing with friction of the skin are general measures of value. The medicinal treatment is that of atonic gastrectasis (see p. 448).

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## ACUTE CATARRHAL GASTRITIS

**Etiology.**—Acute catarrhal inflammation of the stomach is often the result of dietetic errors, as hasty eating or the ingestion of food that is coarse, excessive in quantity, too hot or too cold, or partially decomposed. Overindulgence in alcohol is an important factor in many cases. Certain drugs, even in moderate doses, as the iodides, salicylates, arsenic and the salts of mercury are also capable of inducing the disease.

The sensitiveness of the stomach to the action of irritants varies in different individuals and is exaggerated by all disturbing influences affecting directly or indirectly gastric digestion. Thus, subjects of tuberculosis, anemia, circulatory disorders, and diseases of the stomach other than catarrh are especially predisposed to acute gastritis. Even exposure to cold, fatigue or emotional depression during the period of digestion may render the individual temporarily more susceptible.

A secondary form of acute catarrhal gastritis is sometimes excited by the ingestion of pus or gangrenous material formed in the mouth or air-passages. In most cases, however, secondary gastritis occurs as an accompaniment of one of the acute infections, such as septicopyemia, scarlet fever, erysipelas, or variola, or is the consequence of an auto-intoxication, such as may be caused by nephritis, diabetes or gout. It may also result from the extension of an inflammatory process from one of the adjacent organs.

**Morbid Anatomy.**—Macroscopically, acute catarrhal gastritis is characterized by hyperemia and swelling of the gastric mucosa and an increased secretion of viscid mucus. Minute hemorrhages and erosions may also be present. Microscopically, the chief changes are cloudy swelling of the epithelial elements of the glands and a variable amount of interstitial round-cell infiltration.

**Symptoms.**—The disease presents various degrees of severity. As a rule it sets in with loss of appetite, an unpleasant taste in the mouth, a feeling of discomfort, or even of actual pain, in the region of the stomach, nausea, belching and eructations of fluid, which may be tasteless (waterbrash) or acrid (pyrosis). Headache, vertigo, lassitude and depression of spirits add to the distress. Vomiting soon supervenes in all but the mildest cases and though it often affords relief, it may prove obstinate. The vomit at first consists of partially digested food, together with mucus and fatty acids, and afterwards only of mucus and bile. If the vomiting is persistent and accompanied by much retching there may be slight capillary hemorrhage. Thirst is usually marked and not rarely there is moderate fever, particularly in children. Constipation is the rule, especially at first.

Objectively, the tongue is heavily coated, the breath is foul, the pulse is accelerated, and the region of the stomach is tender and usually distended. Herpes is often present about the lips. The urine is concentrated and on standing deposits urates. Diarrhea may develop from extension of the irritation to the intestines or jaundice from swelling of the duodenal mucosa about the orifice of the common bile-duct.

Uncomplicated acute gastritis almost always terminates favorably, the duration of the disease ranging from a few days to a fortnight. Frequently recurring attacks, however, may result in chronic catarrhal gastritis.

**Diagnosis.**—The diagnosis is usually easy. The history, the acute onset, the favorable effect of the vomiting upon the other symptoms, the character of the vomit, the absence of intense pain and of severe constitutional disturbance, even, in most cases, of fever, and the short duration leave little doubt as to the nature of the disease. The absence of a rash and of other characteristic symptoms in the course of a few days will serve to exclude the *exanthematous diseases of childhood*, and the acute onset, the rapid rise and abrupt fall of the temperature and the absence of epistaxis, of bronchial catarrh, of splenic enlargement, of roseola, and of the Widal reaction will serve to eliminate *typhoid fever*. Other conditions, such as meningitis, the crises of tabes, angina pectoris, acute uremia, vomiting of pregnancy, acute dilatation of the stomach, the various colics, intestinal obstruction, and appendicitis, which sometimes bear a certain resemblance to acute gastritis, are not likely to cause confusion if the patient is carefully examined.

**Treatment.**—If the stomach still contains irritating matter this should be removed at once by lavage or the administration of ipecacuanha by the mouth or of apomorphin hypodermically. The application of a mustard-plaster or of a turpentine stupe over the region of the stomach will aid in relieving distress. As a rule, all food should be withheld for twenty-four or thirty-six hours. At the end of this time, milk and lime-water, pancreatinized milk, or light broths may usually be allowed in small quantities at frequent intervals. The return to solid food should always be effected very gradually. Rectal feeding is rarely required. Thirst is best controlled by the use of cracked ice or, if necessary, by the administration of normal salt solution by the rectum. Rinsing the mouth with cold water at frequent intervals is both grateful and useful.

If there is constipation or any evidence that the irritant has passed into the bowel a mercurial laxative may be given with advantage. Persistent vomiting may be relieved by bismuth subcarbonate (15 grains—1.0 gm.) or cerium oxalate (10 grains—0.6 gm.), combined with phenol (½ minim—0.03 mil), creosote (½ minim—0.03 mil), cocain (⅙ grain—0.01 gm.) or diluted hydrocyanic acid (2 minims—0.1 mil). Morphin is rarely indicated.

## OTHER FORMS OF ACUTE GASTRITIS

**Toxic Gastritis**.—Although the severe forms of catarrhal gastritis are probably always due to the action of some toxic substance, the term toxic gastritis is usually employed to designate inflammation of the stomach resulting from the ingestion of corrosive poisons, such as concentrated mineral acids or caustic alkalies, or of certain poisons, which though non-corrosive, are either very irritant or have the special action of causing fatty degeneration of the glandular epithelium, such as iodin, phosphorus, arsenic, and antimony. The effect of a given poison on the stomach depends not only upon its nature but upon the amount ingested, its concentration, the duration of its action, and the quantity of material already in the stomach. In the case of corrosive poisons the lesions vary from those of acute catarrhal gastritis to the most extensive sloughing of the stomach wall, leading to hemorrhage, to ulceration and occasionally to perforation into the peritoneum. In severe cases if the patient survives the immediate effects of the poison, cicatrization ensues and later there may be stenosis of the pylorus, hour-glass contraction, or other deformity. Phosphorus, arsenic and antimony produce swelling of the gastric mucosa, hyperemia, ecchymoses, and marked fatty degeneration of the glandular epithelium, as well as important changes in other viscera, which often prove more serious than the direct effects of the poison upon the stomach.

*Symptoms.*—In severe cases the onset is sudden and marked by intense burning pain in the throat, esophagus and epigastrium. Vomiting soon occurs and is frequently repeated. The vomitus is usually bloody, and sometimes contains shreds of mucous membrane. Diarrhea may accompany the vomiting if any of the irritant escapes into the intestine. The abdomen, especially the epigastrium, is sensitive to pressure and is often distended. Thirst is pronounced and owing to the dysphagia and persistent vomiting adds much to the patient's suffering. The facial expression is anxious, the surface of the body is cool and covered with perspiration, the pulse is frequent and compressible, the respiration is accelerated and shallow, and the urine is scanty and sometimes albuminous. Convulsions and coma often supervene

toward the close of life in fatal cases. Death may result from shock, perforation of the stomach, or general intoxication. Not rarely, however, the acute symptoms subside and the patient is completely restored in from a week to a fortnight.

In other cases there is only partial recovery, chronic indigestion with more or less malnutrition persisting after the subsidence of the acute symptoms as the result of cicatricial contractions in the stomach or of extensive destruction of its glandular structure.

*Treatment.*—The first indication is to remove the irritant or to neutralize it by administering an appropriate antidote. An emetic may be given, but unless there is evidence of extensive corrosion, siphonage with the stomach-tube is preferable. In many cases the antidote may be given through the tube. In general, acids are neutralized by alkalies (magnesia, chalk, sodium bicarbonate) and egg-albumin, and alkalies by weak acids (vinegar, lemon-juice). Morphin is often required on account of the intense pain. Collapse must be combated by the application of heat to the surface of the body and by the subcutaneous administration of diffusible stimulants. The after treatment is that of the severer forms of acute catarrhal gastritis.

**Phlegmonous Gastritis.**—This rare disease is characterized by suppurative inflammation of the submucous coat of the stomach. Bossart[1] found 110 cases on record in 1912, but this number has been greatly increased in the last few years. Two varieties are observed, the diffuse and the circumscribed. The former is the more common (5 to 1). Adjacent viscera are frequently involved in the phlegmonous process and in more than one-half of the cases purulent peritonitis supervenes. The immediate cause is almost always the streptococcus alone (two-thirds of the cases) or this organism in association with the staphylococcus, the colon bacillus, or the pneumococcus. The invasion may occur through a defect in the gastric mucosa or by way of the blood or lymph channels. Thus, the disease may follow ulcer or cancer of the stomach, it may be secondary to an acute streptococcal infection elsewhere in the body, or it may develop as a part of a general septicopyemia. Rixford[2] has reported 3 cases occurring during an outbreak of streptococcal sore throat. Not rarely, however, phlegmonous gastritis comes on suddenly in apparent health and without obvious cause. In other instances it has been ascribed to alcoholism, dietetic errors, ingestion of poison, or trauma. Males are attacked more frequently than females and the period of greatest incidence is between the ages of 20 and 50 years. The chief symptoms are pain and tenderness in the epigastric region, spreading more or less rapidly to the rest of the abdomen, persistent vomiting of bile-stained fluid, and the usual phenomena of sepsis—chills, fever (100°–104° F.), sweats, leucocytosis, delirium, and collapse. Either constipation or diarrhea may be noted. Occasionally a mass can be felt in the region of the stomach and rarely there is vomiting of pus. Jaundice was present in 16 per cent. of 85 cases analyzed by Leith.[3] Extreme restlessness and anxiety are sometimes prominent features.

Owing to the close resemblance of the clinical picture to that often seen in perforative peritonitis with subphrenic abscess, in abscess of the liver, in suppurative cholecystitis, and in acute pancreatitis the diagnosis is rarely possible during life unless the abdomen is opened. The disease proved fatal, usually in from one to seven days, in more than 90 per cent. of the recorded cases. In several instances recovery has resulted from the spontaneous rupture of the

[1] Korrespondenzbl. f. Schweiz. Aertze, No. 6, 1912.
[2] Ann. Surg., 1917, 66, 325.
[3] Edinburgh Hosp. Rep., 1896, iv.

abscess into the stomach and the complete evacuation of the pus, and in a few cases surgical treatment (free incision and drainage) has been successful. In Bovée's case the patient was a woman six month's pregnant.

**Pseudomembranous Gastritis and Mycotic Gastritis.**—Pseudomembranous gastritis is more common in children than in adults. It may occur in diphtheria or other infectious diseases, or it may follow the ingestion of irritant poisons. The false membrane may appear in small patches on top of the rugæ or it may cover a considerable portion of the stomach, forming, as it were, a cast of the organ. A rare form of gastritis, the mycotic form, is due to the growth of *Oïdium albicans*, *Achorion schönleinii* or the mould-fungi in the stomach. These forms of gastritis have an anatomical rather than a clinical interest and can be recognized during life only by the discharge of false membrane or of the peculiar fungi in the vomit.

## CHRONIC GASTRITIS

(Chronic Gastric Catarrh)

**Definition.**—Chronic gastritis is a chronic inflammation of the mucour membrane of the stomach, often affecting as it progresses the glandulas structure, the interstitial tissue, the submucosa and even the muscular coat of the organ.

**Etiology.**—The disease may be either primary or secondary. The *primary form* is comparatively uncommon. It may result from the frequent ingestion of irritants not sufficiently powerful to cause erosion or even acute inflammation of the mucosa. Under this head may be mentioned alcohol, strong spices, and certain drugs, such as the drastic cathartics. Food itself, if coarse, excessively rich, improperly prepared, over-abundant or poorly masticated may be, and often is, an important factor. Only rarely is the disease the direct sequel of acute gastritis.

As a *secondary condition,* chronic gastritis may develop in the course of some other chronic disease of the stomach, such as cancer, ulcer, or gastrectasis. It may result from venous congestion due to cirrhosis of the liver, chronic heart disease, etc. It is also met with in various general diseases that vitiate or impoverish the blood, such as tuberculosis, diabetes, nephritis, and pernicious anemia.

**Morbid Anatomy.**—The mucous membrane is of a grayish or slaty color, and is often covered with tenacious mucus. The veins are usually dilated, and there may be small areas of pigmentation or hemorrhage, or, less frequently, of superficial erosion. Microscopically, the lesions are those of interstitial inflammation with hypertrophy or atrophy of the parenchymatous tissue. In one form—*hypertrophic or productive gastritis*—the mucous membrane is thickened and wrinkled or slightly granular, and microscopic examination shows pronounced hyperplasia of the deeper glandular elements and interglandular infiltration of small round cells. Actual fibrosis is not often seen.

Occasionally, the proliferative process results in the formation of a greater or less number of wart-like excrescences, and to this condition the term "gastritis polyposa" has been given. Although accurate observations are lacking, it is probable that hypertrophic stenosis of the pylorus in adults is a result of chronic productive gastritis, especially marked at the pylorus. In another form of the disease—*atrophic gastritis*—the mucous membrane

is smooth, like that of the bowel, and the entire wall of the stomach is more or less thinned. Microscopically, the number of tubules is diminished and the cells of those that remain show varying degrees of mucoid degeneration.

Between the tubules there is round-celled infiltration or, if the case is far advanced, an overgrowth of connective tissue. It is usually assumed, but without much evidence, that this form represents a late stage of hypertrophic gastritis.

The benign form of *plastic linitis* (cirrhosis of the stomach)—a condition in which the wall of the stomach is enormously thickened and the lumen of the organ is much reduced—is regarded by some authorities as a form of chronic gastritis, in which atrophy of the gastric tubules is associated with excessive hyperplasia of the submucous connective tissue.

**Symptoms.**—Chronic gastritis presents various aspects according to the character, degree and stage of the inflammatory process, and also the presence or absence of complications. Owing to the power of the small intestine to perform alone all the processes of digestion, mild forms of the disease may cause little disturbance if the motility of the stomach is good, the functions of the small intestine are intact, and the food is unirritating. In many cases, however, eating is followed by epigastric distress, which occasionally amounts to actual pain. As a rule, solids excite more discomfort than liquids. Flatulence, heartburn, belching and eructations are often present. Nausea is also common, but vomiting is rather unusual except in the more advanced forms of the disease. Vomiting of mucus early in the morning is a well known feature in the chronic gastritis of drunkards, but the mucus in this so-called *vomitus matutinus*, as Boas has shown, usually comes from the throat rather than from the stomach. If vomiting occurs after meals the vomited matters consist of partially digested food intimately mixed with more or less thick ropy mucus. The appetite may be normal or even inordinate, but in the majority of cases it is diminished or easily satisfied. Increased thirst is not infrequent. In many cases, probably from coexisting pharyngitis, the tongue is coated, the breath is fetid, the taste is perverted, and the secretions of the mouth are deranged. Constipation is the rule, although this condition may alternate with diarrhea. In atrophic gastritis diarrhea is sometimes a serious symptom. Other subjective symptoms are headache, dizziness, palpitation and malaise.

In uncomplicated cases physical examination of the abdomen rarely reveals any abnormalities, except, perhaps, a diffuse sensitiveness to pressure in the region of the stomach. Analysis of the gastric contents is more important. The secretion of hydrochloric acid varies. In hypertrophic gastritis it is usually normal or increased (gastritis acida), and in atrophic gastritis it is nearly always diminished (gastritis subacida). In advanced cases of atrophic gastritis there may be an absence of both hydrochloric acid and enzymes (achylia gastrica). The most suggestive objective finding, however, is the presence of an excessive amount of mucus, not only after a test meal, but also in the morning before breakfast, although one must be sure that the mucus has really been formed in the stomach itself. Mucus that has been swallowed, unlike that derived from the stomach, is not, as a rule, intimately mixed with the food, but occurs in the form of discrete lumps or as foamy masses that float on the surface of the wash-water. Sediment obtained in the morning from the fasting stomach may contain shreds of the gastric mucosa showing hyperplasia of the glands and little degeneration of the individual cells, or, on the other hand, a dearth of glands and pronounced degeneration of the cells. The motor power of the stomach is often normal, but it may be either decreased or increased. Actual gastrectasis is not

common, but it may be present as the cause or as a sequel of the catarrhal process or as an unrelated accompaniment of the disease.

**Diagnosis.**—The diagnosis may be difficult, as no one symptom is characteristic and as almost the entire symptom-complex may result from a neurosis or an organic disease of the stomach other than gastritis. In many instances the patient will have to be kept under observation for a long time and the stomach-contents repeatedly examined before other conditions can be excluded.

In *simple atony of the stomach* fluids excite as much distress as solids, vomiting is rare, the secretion of mucus is not increased, the secretion of hydrochloric acid is usually normal, remnants of food are to be found in the stomach seven hours after a test-meal, and the region of the stomach is not tender. In *nervous dyspepsia* the severity of the symptoms varies considerably from day to day according to the mental state of the patient, and is not materially influenced by the quantity or quality of the food; the secretion of acid is normal or subject to sudden variations at short intervals, and there is no excess of mucus.

It may be difficult or impossible to differentiate gastritis from the early stage of *carcinoma of the stomach.* Sooner or later, however, the latter will be revealed by the continued loss of weight, secondary anemia, persistent achlorhydria, frequent vomiting, hematemesis, occult bleedings and the presence of a filling defect in the contour of the stomach on x-ray examination. The differentiation of diffuse cirrhosis of the stomach (plastic linitis) from carcinoma has rarely been made during life.

The exclusion of *peptic ulcer* is not usually difficult. In the latter there is a regular recurrence of actual pain from half an hour to three hours after meals, alkalies, food or vomiting relieve the pain, hematemesis or occult bleeding may occur, tenderness is often definitely localized, after lasting from a few days to many weeks the symptoms often completely disappear to reappear at varying intervals, and x-ray examination, as a rule, yields characteristic signs, such as a niche or accessory pocket in gastric ulcer and bulbar deformity in duodenal ulcer.

About the only points of distinction between acid gastritis and *simple hyperchlorhydria* are the presence in the former of an excess of mucus in the gastric contents and of fragments showing hyperplasia of the glandular elements in the gastric sediment.

The diagnosis of chronic gastritis having been made it still remains to be determined whether the disease exists as an independent condition or whether it is present as a result of changes in one of the other organs, such as the liver or heart, or of some constitutional disturbance.

**Prognosis.**—Under a suitable diet and proper treatment mild forms of primary chronic gastritis are frequently cured, at least in the clinical sense. Relapse, however, is common. The outlook for complete recovery is poor if with the catarrh there is much atony of the stomach or extensive atrophy of the gastric mucosa. In the secondary form of gastritis the outcome will depend in large measure, of course, upon the nature and severity of the primary disease.

**Treatment.**—The cause should be ascertained and removed if possible. Regularity in the time of meals and thorough mastication of food must be insisted upon. The patient should be cautioned against overeating and the drinking of large quantities of liquid, especially iced water, during meals. The resumption of mental or physical work immediately after meals must also be avoided. Change of scene, with freedom from business worry or household cares, and properly regulated exercise in the open air are often most desirable.

In general a mixed diet of soft, pulpy, or finely divided food should be prescribed. It may include, as a rule, boiled, baked or grilled beef and mutton, boiled or baked chicken, boiled fish, stewed sweet-breads, soft-boiled or poached eggs, well-cooked rice, purée of potato, green peas or spinach, stale bread, fresh butter, calve's-foot jelly, junket and light puddings. Pork, veal, smoked fish, fried foods, coarse vegetables, rich soups, strong spices, cheese, raw fruits, pastry, and sweetmeats should be avoided. Alcohol is inadmissible and tea, coffee and cocoa should be used sparingly, if at all. Ordinarily three meals a day will suffice, but if the motor power of the stomach is much impaired it is better to give small meals at frequent intervals. In advanced cases, provided there is no marked atony of the stomach, it may sometimes be advisable to restrict the diet to milk or to milk with gruel, meat-jellies and minced beef. The milk (about two quarts in the 24 hours) should be taken at regular intervals and preferably diluted with lime-water.

Lavage of the stomach before breakfast may be of service if there is excessive secretion of mucus, otherwise this procedure should be reserved for the exceptional cases in which stagnation of the stomach-contents is present as a complication. Simple luke-warm water, a 1 per cent. solution of sodium chloride, or 5 per cent. solution of sodium bicarbonate may be employed for the purpose. In some cases the sipping of a glassful of hot alkaline water half an hour before meals proves an efficient and agreeable substitute for lavage.

In chronic gastritis with subacidity, dilute hydrochloric acid, in doses of 10 minims (0.6 mil) gradually increased to 15 minims (1.0 mil), in a wine-glassful of water, taken through a glass tube, during or at the close of the meal is often of service. As such doses of the acid rarely suffice to compensate for the existing deficiency in acid secretion it is likely that the drug merely acts as a stomachic. Digestive ferments, such as pepsin and pancreatin, need not be given unless there is evidence of atrophy of the gastric follicles. The addition of a bitter—nux vomica or gentian—to the acid, however, is sometimes advantageous, especially if the appetite is poor or the stomach is atonic. If the stomach is irritable, bismuth subnitrate, in doses of 20–30 grains (1.3–2.6 gm.), suspended in water and taken half an hour before meals, is useful. If however, the irritability is associated with hyperacidity, better results may be secured by giving an antacid powder, such as the following, from ½ to 1 hour after meals:

℞. Bismuth subcarbonatis..... gr. ccl (16.0 gm.)
Sodii bicarbonatis..... gr. cc (12.5 gm.)
Magnesii oxidi..... ʒiss (6.0 gm.).—M.
Ft. Chart. No. xx.
Sig.—One powder suspended in water half an hour after meals.

Not rarely when the stomach is especially sensitive a short course of silver nitrate is of benefit. It may be given in pill form with extract of hyoscyamus, as in the following formula:

℞. Argenti nitratis..... gr. vii (0.5 gm.)
Extracti hyoscyami..... gr. xii (0.8 gm.).—M.
Fiant pilulæ No. xx.
Sig.—One pill half an hour before meals.

Flatulence, if not relieved by appropriate diet, may yield to the administration of antifermentatives, such as creosote or phenol, in small doses. So far as possible, constipation should be overcome by regulation of the diet, exercise, massage and perhaps the occasional use of laxative enemas or

suppositories. Should these measures fail sodium phosphate, Rochelle salt or artificial Carlsbad salt may be given in small doses in the early morning, preferably in hot water. Drastic purgatives of all kinds are contraindicated.

## PEPTIC ULCER

**Definition.**—The term peptic ulcer is applied to a circumscribed loss of substance in the stomach or duodenum, frequently involving both the mucous membrane and the deeper structures and caused by reduced resistance of the tissues to the digestive action of the gastric juice.

Similar lesions are occasionally found in other parts of the digestive tract to which the acid chyme may gain access, namely, in the cardiac end of the esophagus and, after gastrojejunostomy, in the jejunum.

**Etiology.**—Owing to the uncertainty in diagnosis in many cases and the fact that acute ulcers may heal without leaving scars, the *incidence* of the disease is probably greater than either clinical studies or necropsy records indicate. Based on postmortem findings, however, it appears to be between 1 and 2 per cent. in this country and between 4 and 5 per cent. in England and on the Continent. Although peptic ulcer may occur at any *period of life* from infancy to old age, the large majority of cases are first recognized between the ages of 20 and 45. Lockwood[1] has collected 125 cases of gastric ulcer in childhood, and Schmidt[2] found 37 cases of duodenal ulcer in 3824 necropsies in chlidren.

Gastric ulcer is about as common in one *sex* as the other, but duodenal ulcer is 4 or 5 times more frequent in males than in females. The assumption that the occurrence of peptic ulcer is favored by *occupations* entailing the pressure of solid bodies against the epigastrium has little trustworthy evidence to support it. *Impairment of the general health* from anemia, particularly chlorosis, cardiovascular disease, tuberculosis, alcoholism, dietetic errors, unhygienic surroundings, etc., is an important etiologic factor. Moynihan, Mayo, Paterson, Deaver and other surgeons have drawn attention to the frequent coexistence of peptic ulcer and *chronic inflammation in the appendix, colon* or *gall-bladder*. In nearly two-thirds of 140 cases of gastric ulcer reported by Smithies[3] from the Mayo clinic either chronic appendicitis or cholecystitis was demonstrated as a concomitant process. As Curling[4] first pointed out, extensive *burns* of the skin may be followed within a few days by acute ulceration of the duodenum. The cases arising from this cause, however, are comparatively few. Another occasional factor is *physical injury* in the region of the stomach.

**Pathogenesis.**—The exact conditions that must obtain before the gastric juice can attack the tissues of the stomach or duodenum is not definitely known. It is probable, as Virchow[5] suggested, that in certain instances embolism or thrombosis, with or without antecedent disease of the occluded vessel, is an important factor. Local injury (mechanical, thermal or chemical) may also explain some cases. Irritation of the vagus nerve, with consequent muscular spasm and ischemia, has frequently been cited as a possible cause (Talma, Westphal, Eppinger and Hess). Recently the view, originally

[1] Surg., Gynec. and Obstet., 1914, xix, 462.
[2] Berlin. klin. Woch., 1913, l, 593.
[3] Amer. Jour. Med Sci., Mar., 1913.
[4] Med.-Chir. Trans., 1842, xxv.
[5] Virchow's Arch., 1855, v.

expressed by Böttcher, that bacterial infection or intoxication may play a part in the genesis of peptic ulcer has received considerable attention. Rosenow[1] has produced gastric ulcers in dogs by intravenous injections of certain strains of streptococci. In the case of ulceration following burns of the skin it is assumed that poisons formed in the burned tissue escape by way of the duodenum and damage the mucosa. Experimental evidence can be adduced in support of all these theories. Ulcers produced artificially, however, are almost always acute and heal rapidly, and, therefore, even if the genesis of the peptic ulcer were satisfactorily explained the cause of its chronicity would still remain obscure. Hyperchlorhydria, upon which much stress has been laid, may sometimes play a part in maintaining the ulceration, but as it is not constantly present, it cannot be the only factor. Recently, it has been suggested that an anti-enzyme which is normally present and resists peptic or tryptic digestion is deficient or absent in these cases.

**Morbid Anatomy.**—*Minute abrasions* or *hemorrhagic erosions* of the mucous membrane of the stomach are not uncommon and may occur in acute infections, chronic circulatory diseases, cachectic states and after abdominal operations of various kinds, especially operation for appendicitis with septic complications. These lesions, which are probably of toxic or embolic origin, are not essentially different from the acute forms of gastric ulcer, although they are clinically unimportant, except in the rare instances in which they invade a vessel of considerable size and cause copious or, perhaps, fatal hemorrhage.

The peptic ulcer itself may be acute or chronic. The *acute ulcer* is usually small, superficial, rounded, with a soft clean-cut margin and a smooth floor. It is more commonly gastric than duodenal, and while it may be situated in any part of the stomach, it is most frequent near the pyloric end of the organ. In about 20 per cent. of the cases more than one ulcer is present. The acute ulcer tends to heal quickly and apparently does not often lead to the chronic from (Mayo, Moynihan).

The *chronic peptic ulcer* is usually larger than the acute form, sometimes attaining a diameter of several centimeters, and is often irregular in outline. It has an indurated wall-like margin, and is frequently cone-shaped, the defect being largest in the mucosa and tapering toward the serosa as by a series of terraces. The floor may be the submucous, muscular or peritoneal coat of the stomach, or even some adjacent viscus. From 5 to 10 per cent. of chronic gastric ulcers are multiple. Duodenal ulcers are usually solitary. However, in 2.3 per cent. of 629 cases treated surgically in the Mayo clinic[2] both gastric and duodenal ulcer were found. The solitary chronic ulcer, whether gastric or duodenal, is situated in the large majority of cases within an inch or two of the pyloric ring.

A common form in the stomach is the "saddle ulcer" extending from the lesser curvature above the pylorus flap-like down the anterior and posterior wall. More than 90 per cent. of duodenal ulcers are in the first portion of the duodenum and on the anterior surface. Formerly duodenal ulcer as compared with ulcer of the stomach, was considered rare, the ratio being variously stated as between 40 to 1 (Andral) and 10 to 1 (Fenwick), but now operators of experience regard it as commoner than gastric ulcer, estimating the ratio as 2 to 1 (Robson, Mayo) or 5 to 1 (Moynihan).

**Events.**—*Perforation* is one of the most serious and common complications. Occurring on the anterior surface of the stomach or duodenum, and in the absence of protective adhesions, it may set up *general peritonitis* or

[1] Jour. Amer. Med. Assoc., April 19, 1913; Sept. 12, 1914; Nov. 13, 1915.
[2] Amer. Jour. Roent., 1917, iv, 552.

kill suddenly through shock. Occurring on the posterior aspect of the stomach or duodenum, especially if adhesions have already formed, it may lead to localized acute peritonitis with the formation of a *subphrenic abscess*. After such an abscess has fully developed it may approach the surface beneath the right costal margin, at the umbilicus, behind the kidney, or in the cecal region, thus simulating appendicitis; or it may rupture into the peritoneal cavity, or into one of the adjacent organs, as the liver, gall-bladder, pancreas, colon, or even into the pleura, pericardium or heart. An occasional result of perforation is the formation of a *gastrocutaneous fistula*. When an ulcer advances slowly towards the surface, localized peritonitis ensues, leading to *adhesions* (plastic perigastritis) between the stomach and adjacent viscera. These adhesions may result in various deformities of the stomach, intestinal obstruction, persistent jaundice, or cystic or other disease of the pancreas.

*Hemorrhage* in the form of hematemesis or melena occurs in a large proportion of cases. Persistent oozing may give rise to intense secondary anemia, while copious extravasation from the erosion of a large vessel may be the immediate cause of death. The transformation of gastric ulcer into *gastric cancer*, suspected by Rokitansky, is now known to be a common occurrence. As to the frequency of this transformation, however, opinions differ. The highest figures are those of Robson, Mayo and Moynihan, who hold that from one-half to two-thirds of the cases of gastric cancer are due to ulcer. Ulcers of the duodenum rarely become cancerous.

*Cicatrization* occurs in many cases producing, if the ulcer is a large one, a dense stellate scar. An extensive cicatrix may occasion, according to its location, *stenosis of the pylorus*, *gastrectasis*, *hour-glass contraction of the stomach* or *stricture of the duodenum*. Gastrectasis may occur also as the result of pylorospasm or perigastric adhesions. Horgan[1] has drawn attention to the frequent association of peptic ulcer and *chronic pancreatitis*.

Among exceptional complications may be mentioned *acute pancreatitis* (Körte[2]), *adhesive* or *suppurative pylephlebitis* (Bryant[3]), *parotitis* (Hone[4]), *phlegmonous gastritis* (Merkel, v. Mintz) and *tetany* (Riegel).

**Symptoms.**—The clinical picture varies. The ulcer may run its course without definite symptoms and undergo healing by cicatrization or be discovered accidentally at the necropsy; it may remain latent for an indefinite period and finally be announced by symptoms of hemorrhage or perforation; or, as is generally the case, it may occasion a symptom-complex in which the usual phenomena of indigestion appear and are followed after an interval of weeks, months or years by such definite indications as pain, tenderness, vomiting, hemorrhage, and hyperchlorhydria.

The appetite is, as a rule, good, although it is often lost during acute attacks of pain, and many patients refrain from eating for fear of bringing on discomfort. The tongue is usually clean or only moderately coated. The bowels are, as a rule, sluggish. *Loss of weight* occurs in about three-fourths of the cases, and may be ascribed to insufficient food, vomiting, hemorrhage or pain. Even when it is pronounced, there is rarely cachexia. A variable degree of *chloranemia* is usually observed either as a concomitant condition or as a sequel of the ulcer. In hemorrhagic cases the hemoglobin often falls to 50 per cent. or lower.

*Pain* in the epigastrium, sometimes radiating to the back or side, is the most constant symptom and usually the one for which the patient first seeks

[1] Collected Papers of the Mayo Clinic, 1919, xi.
[2] Archiv. f. klin. Chir., 1912, No. 3.
[3] Guy's Hosp. Rep., vol. lvi.
[4] Austral. Med. Gaz., 1898.

advice. It does not come on immediately after eating, as a rule, but in from one-half to three or four hours after the meal, and is variously described as being of an aching, cutting, boring or burning character. The pain varies in intensity according to the character of the food and sometimes according to the posture that the patient assumes. Occasionally it takes the form of a veritable colic (pylorospasm) severe enough to demand the use of morphin. The interval after eating at which it occurs is generally constant in each case, being longer, as a rule, with duodenal than with gastric ulcer. In the case of duodenal ulcer it commonly appears at a time when the patient should be beginning to feel hungry for the next meal and hence it has come to be known as the "hunger-pain." The pain is usually eased by bland food, by alkalies, and by vomiting or lavage. Pressure generally increases it, but may afford relief. Another peculiar feature of the pain, particularly in duodenal ulcer, is its periodicity. At the onset of the disease the patient may suffer only for a few days or weeks and then be comfortable for several months or even for one or two years. The intervals, however, tend to become shorter and at last the discomfort may be almost constant. The periods of pain often bear a seasonal relation and may be ushered in by indiscretions in eating, by mental stress, or even by chilling of the body. With the pain there is frequently an *area of tenderness* in the epigastrium, usually to the right of the midline. In some cases an area of tenderness is found also posteriorly to the left of the tenth dorsal vertebra (Boas' point).

*Vomiting* is another important symptom, especially in gastric ulcer involving the pylorus. In duodenal ulcer it is often absent. In most cases it occurs at the height of the pain, the average time being 2 or 3 hours after meals. The vomited matter usually consists of sour fluid and fine particles of food, and, unless there is marked hypersecretion or gastrectasis, it is rarely abundant. The vomiting of ulcer soon disappears, as a rule, when the patient is kept in bed and fed on liquid food.

*Hemorrhage* in the form of actual hematemesis or melena occurs at one time or another in about 25 per cent. of the cases and is the immediate cause of death probably in 3 or 4 per cent. of the cases. The presence of blood in the stools is readily overlooked and statements of patients on this point are frequently unreliable. The vomited blood is usually fluid and, unless very abundant and quickly ejected, is of a brown-black color. If the blood remains in the stomach for some time the vomit may have the "coffee-ground" appearance so commonly seen in gastric cancer. Some blood nearly always passes into the bowel and in the case of duodenal ulcer all of it may be discharged with the stools, imparting to them a black, tarry appearance. Copious bleeding gives rise to faintness, pallor, sweating and prostration, and, if the patient survives, is followed by the usual signs of intense anemia. Even when there is no visible hemorrhage from the stomach or bowel, minute traces of blood can often be detected by chemical means (*occult hemorrhage*) in the vomit or feces, especially in the latter. (For chemical tests and sources of error see p. 439.)

The concentration of inorganic acidity in the gastric contents varies. In many cases, but in a less proportion than was formerly believed, the *concentration of both total and free HCl is high.* The increase is more constant in duodenal than in gastric ulcer. In at least 50 per cent. of gastric ulcers the acidity is well within the normal range.

In addition to localized tenderness, physical examination not infrequently reveals *rigidity* of the right rectus muscle, especially during acute exacerbations. In chronic cases, if the abdominal wall is not too rigid, an area of slight induration is occasionally palpable in the epigastrium and may be mis-

taken for a true neoplasm. It signifies inflammatory exudation, adhesions, or muscular hypertrophy. In about one-half the cases of gastric ulcer food retention is observed after the twelve-hour period. In duodenal ulcer food retention is somewhat exceptional, but not rarely an excess of highly acid gastric secretion is found in the fasting stomach.

In the majority of cases of peptic ulcer the roentgen ray is an indispensible aid to diagnosis. In gastric ulcer the following signs may often be observed singly or in various combinations on the plate or screen or on both: The niche, or recess of the ulcer projecting from the peripheral outline of the stomach; an accessory pouch or pocket produced by penetration of the ulcer into adjacent tissues; organic hour-glass constriction, the result of cicatricial contraction or external adhesions; spasmodic contractions, especially the local indentation known as the incisura and the spastic hour-glass stomach; a definite residue in the stomach from the six-hour barium meal, as a consequence of local spasm, cicatricial contraction or hypotonus (50 per cent. of the cases); and various abnormalities of peristalsis. The important roentgenologic indications of duodenal ulcer are distortion of the duodenal bulb or cap, probably as a result of local spasm; hypertonus; exaggerated peristalsis (60 per cent. of the cases) and a reduction of the emptying time of the stomach (hypermotility).

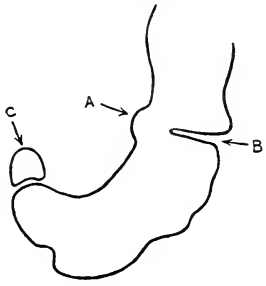


FIG. 13.—Ulcer crater at A, incisura opposite at B, normal bulb at C.

FIG. 14.—Incisura type of bulbar deformity.

*Perforation* occurs in from 5 to 10 per cent. of the cases. It may be acute or subacute. Acute perforation is characterized by the sudden occurrence of severe, agonizing pain in the epigastrium, intense board-like rigidity of the recti, especially of the right one, exquisite tenderness, embarrassed respiration, vomiting, pallor and prostration. Collapse is usually not present before the occurrence of diffuse peritonitis and this is true also of abdominal distention. Obliteration of the liver dulness has little significance and the occurrence of dulness in the flanks is by no means common. Owing to the tendency of the fluid to gravitate into the right iliac fossa, appendicitis may be closely simulated. The previous history, however, is usually distinctive. In acute intestinal obstruction the pain is more likely to be of a cramp-like character and less localized than in perforation, the board-like rigidity of the abdominal wall is lacking, constipation is absolute and the vomitus is usually stercoraceous. In acute pancreatitis the antecedent history more frequently suggests cholelithiasis than peptic ulcer, symptoms of profound collapse show themselves almost immediately, and the skin, as Halsted and Moynihan have pointed out, has often a peculiar leaden or cyanotic hue.

Ectopic pregnancy with rupture of the tube may usually be distinguished by absence or irregularity of the menstrual periods immediately before the rupture, limitation of the pain and rigidity to the lower part of the abdomen, signs of internal hemorrhage (great pallor, air-hunger, sighing, restlessness, bluish discoloration of the navel, etc.) and detection by vaginal examination of swelling or resistance to one side of the womb.

In subacute perforation of the stomach the symptoms are less severe, the clinical picture being that of localized abscess, frequently subphrenic, with the usual phenomena of systemic infection.

*Perigastric adhesions* are found at autopsy in from 40 to 50 per cent. of the cases (Fenwick, Robson, Hale White). The organs most frequently involved with the stomach are the pancreas, liver and colon. Fixation of the stomach to the anterior abdominal wall is exceptional. The character and severity of the disturbances vary with the location and extent of the adhesions. Gastrectasis and hour-glass stomach are among the possible complications. The most common symptom of adhesive perigastritis *per se*, however, is pain, constant or paroxysmal, and often persisting for years. In many cases the pain is not influenced by taking food, but is aggravated by physical exertion, and is relieved by rest, especially in the recumbent position, and also, to some extent by the application of an abdominal binder. Physical examination may reveal local tenderness and occasionally an indefinite mass. The general health is often unaffected.

*Organic hour-glass* constriction of the stomach is caused in the majority of cases by the cicatrization of a girdle ulcer. It may be a result, however, of gastric carcinoma, gastric syphilis, or perigastric adhesions, and in rare instances it is probably congenital. Moynihan and others attach importance to the following signs: the persistence of the succussion splash after the stomach has been apparently emptied by the tube; the escape of turbid fluid through the tube a few minutes after the stomach has been apparently washed clean (Wölfler); the return of only a portion of the fluid after the introduction of a measured quantity into the stomach (Wölfler); the occurrence of a bubbling or gurgling sound two or three inches to the left of the midline on alternately compressing each side of the abdomen after the administration of a Seidlitz powder in two portions (von Eiselsberg); and appearance of a bulging first on one side of the epigastrium and then on other, with perhaps a distinct sulcus between the two, after inflation of the the stomach with $CO_2$ (von Eiselsberg, Schmid-Monnard). Although the positive results with these various tests have more or less diagnostic value, Roentgen ray examination after a bismuth or barium meal is by far the best clinical method of determining the presence or absence of hour-glass deformity. The organic form of hour-glass stomach, as visualized by the x-ray, may, however, be closely simulated by the spasmodic form, arising from a lesion of the stomach itself or from sources outside of the stomach (chronic appendicitis, chronic cholecystitis, etc.), but in the latter the constriction is likely to be intermittent, inconstant in location, of greater depth than width, and to be effaced by general anesthesia or the administration of atropin or belladonna in full doses.

**Diagnosis.**—It is often impossible to differentiate *gastric* from *duodenal ulcer* without the aid of the x-ray, and even this occasionally fails. One may suspect a duodenal ulcer, however, if the symptom-complex is definitely periodic and the intermissions are relatively long, if the pain appears late after eating and is eased completely by the next meal or by food between meals, and if the degree of gastric acidity is especially high. It is seldom possible to distinguish clinically between gastric ulcer and minute *erosions*

of the gastric mucosa with hematemesis. In *simple hyperchlorhydria*, as contrasted with peptic ulcer, the pain is not accompanied by areas of tenderness, nor by bleeding, vomiting is exceptional and the characteristic roentgenographic signs of ulcer are absent. In *cholecystitis* the painful attacks usually appear very abruptly, at irregular intervals and without reference to the ingestion of food, are not relieved by alkalies or by eating, and are frequently accompanied by chill, slight jaundice and tenderness over the gall-bladder or liver. Vomiting of green or yellowish fluid may occur, but it affords less relief than in ulcer. In *chronic gastritis* the pain is, as a rule, less pronounced and more diffuse, hemorrhage is rare, the vomitus frequently contains much mucus and the x-ray examination proves negative. The distinguishing features of *gastric carcinoma* are considered on p. 441. The differential diagnosis between peptic ulcer and the *crises of tabes*, *Dietl's crises of movable kidney*, and the *pains of spinal disease* should not present formidable difficulties if the patient is thoroughly examined and the history is carefully considered.

**Prognosis.**—In acute cases the tendency is toward rapid recovery, commonly within a few weeks. Chronic ulcers often persist for years without any signs of healing. The mortality is not definitely known, but it has been estimated at 8 or 10 per cent. The percentage of permanent recoveries under any method of treatment is somewhat difficult to determine, as long periods of latency occur in many cases and may readily be mistaken for actual cure. Recurrences are also common and may take place after several years.

**Treatment.**—Prolonged rest and an appropriate diet are the most important factors in the medical treatment of peptic ulcer. In chronic ulcer the rest should be kept up for from 6 to 10 weeks or even longer, and for the first 3 or 4 weeks of this period the patient should be confined to bed. As to the dietetic treatment various plans have been suggested, but none is suitable for every case. A method of procedure that is successful in many instances consists in rectal feeding or in the use of saline or glucose (5–10 per cent.) enemas (250 mils), by rectal drip, three times a day, for the first 3 or 4 days, followed by the administration of milk and cream and soft food in increasing amounts by the mouth. During the period of rectal feeding ice may be held in the mouth, if there is much thirst, but no water should be swallowed. To lessen the risk of parotitis the mouth may be washed at frequent intervals with an antiseptic solution. When feeding by the mouth is resumed it is advisable to begin with milk or albumin-water, giving at first not more than 2 or 3 ounces every two hours. If milk is selected it should be diluted with lime-water. In the course of a few days cream, cream soups, beef juice, soft boiled eggs and well-cooked gruel may also be given. At the end of two or three weeks the intervals between the meals may be increased to three hours, and such articles as milk toast, boiled sweetbread, scraped beef, tender parts of oysters, white meat of chicken, vegetable purées, and custard pudding may be allowed. After 6 or 7 weeks tender beef or mutton, boiled fish, steamed rice, stale bread without crust, and a liberal quantity of butter may usually be added. The return to the ordinary mixed diet, with three meals a day, must be effected with caution and for at least a year after recovery coarse and rich food of every kind, as well as acids and spices, should be avoided.

The plan of treatment devised by Sippy[1] often yields good results when the gastric acidity is high. It aims at reducing the acid content by appropriate food and alkalies every hour during the greater part of the day and the removal at night of any products of continuous hypersecretion. In cases of

[1] Musser and Kelly: Practical Treatment, 1912, vol. iii, 346.

ulcer accompanied by persistent vomiting, duodenal feeding by means of the special Einhorn tube and syringe has its advocates .

The most useful drugs are the alkalies, the insoluble salts of bismuth, and silver nitrate. The alkalies are of service in reducing acidity and lessening motor activity. Sodium bicarbonate is one of the best; it should be given midway between each feeding and may be combined with magnesia or bismuth subcarbonate. A dose of from 10 to 15 grains (0.6–1.0 gm.) of each is usually sufficient. Carlsbad salt (sodium chlorid, 1 part; sodium bicarbonate, 2 parts; and sodium sulphate, 5 parts) is an excellent alkaline laxative of which a teaspoonful or more may be taken in hot water in the early morning. The bismuth salts and silver nitrate act as protectives. From 15 to 20 grains (1.0–1.3 gm.) of bismuth subcarbonate, stirred in water, may be given on an empty stomach several times a day. As an alternate silver nitrate may be given in doses of $\frac{1}{4}$ to $\frac{1}{2}$ grain (0.016–0.03 gm.), three or four times a day, before eating. Extract of belladonna or of hyoscyamus makes a good excipient for the silver salt. If the pain is especially severe belladonna itself may be given in doses sufficient to produce a definite physiologic effect. By depressing vagus, it lessens both the motor and secretory functions of the stomach.

Iron, preferably in organic form, is useful in combating anemia. As it is not improbable that infection plays a part in producing and maintaining peptic ulceration, septic foci in the gums, about the roots of the teeth, or in the tonsils should always receive appropriate treatment. In the event of severe hemorrhage a light ice-bag should be placed over the stomach, morphin should be administered hypodermically, and from 20 to 30 drops of a 1 : 1000 solution of adrenalin should be given by the mouth every twenty minutes for two or three doses. The application of firm bandages to the four extremities may act favorably. Ewald and Minkowski have recommended irrigation of the stomach with ice-water, and Weil and Rodman lavage with hot water (120°–130° F.). Collapse from hemorrhage will require the external application of heat, transfusion of blood or subcutaneous or intravenous injections of salt solution, and the hypodermic injection of diffusible stimulants. Probably no single hemorrhage, whatever its quantity, warrants immediate surgical intervention, and certainly in no case should an operation be done during the bleeding.

*Surgical Treatment.*—In all cases of acute perforation an operation should be done at the earliest possible moment. Patients treated surgically within 6 hours usually recover, while the large majority of those operated on after 12 hours die. Chronic perforation with perigastric abscess or an accessory pocket, persistent stenosis of the pylorus, organic hour-glass constriction of the stomach, repeated copious hemorrhages, any indication of carcinomatous change, and the continuance of the symptoms after a thorough trial of appropriate medical treatment are also definite indications for operative treatment. Whether the surgical procedure shall consist of gastro-enterostomy, partial gastrectomy or pyloroplasty must be determined by the situation and extent of the ulcer. At the Mayo Clinic the operative mortality in 545 cases of gastric ulcer was 4.5 per cent. and in 1684 cases of duodenal ulcer, 2 per cent. Moynihan,[1] reports 808 operations for gastric or duodenal ulcer with a mortality of 1.23 per cent. Operations by competent surgeons afford complete and lasting relief in about two-thirds of all cases. Gastro-enterostomy sometimes fails owing to the occurrence of ulceration at the site of the anastomosis, the development of a jejunal ulcer below the anastomosis, the persistence of the original ulcer, occlusion, of the artificial stoma, or the formation of adhesions. Whatever surgical procedure is

[1] Brit. Med. Jour., Aug. 28, 1920.

employed, it is absolutely necessary to continue treatment along medical lines for several months after the operation or until permanent cure is assured.

## CARCINOMA OF THE STOMACH

**Incidence and Etiology.**—From 25 to 40 deaths per 1000 are from carcinoma, and about 35 per cent. of all carcinomas arise in the stomach.

*Age.*—Nearly three-fourths of the cases occur between the ages of 40 and 70 years. The disease is uncommon in youth and extremely rare in childhood. Osler and McCrae[1] found 13 cases recorded in the second decade and 6 in the first decade. Of 3,257 collected cases 2.5 per cent. occurred in patients under the age of 30. In two or three instances the tumor appears to have been congenital. As regards *sex*, males are affected somewhat more frequently than females. The percentage of cases in negroes is much less than that in whites. *Locality* seems to exert some influence. Thus, the disease is especially common in Switzerland and the region of the Black Forest, and is comparatively rare in Egypt and many other tropical countries. *Occupation* and *mode of life* are apparently without effect on the genesis of the disease. The investigations of Pearson and Guillot, although not conclusive, indicate that *heredity* is an important factor. *Trauma* has only occasionally been recorded as a predisposing cause. *Ulcer of the stomach* undoubtedly increases the predisposition to cancer. The areas of the stomach most commonly affected by the one process are also most commonly affected by the other. Opinions differ, however, as to the frequency with which cancer develops on the basis of an ulcer. Some surgeons of large experience, as Robson, Moynihan and Mayo, estimate it at 60 or even 70 per cent., which is considerably higher than most internists are willing to accept. Duodenal ulcer, unlike gastric ulcer, is rarely productive of cancer. Other affections of the stomach, such as chronic catarrh, atony, etc., are apparently without etiologic influence.

**Morbid Anatomy.**—Carcinoma of the stomach in the vast majority of cases is primary, and develops from the glandular tissue of the gastric mucosa. Rarely it is secondary arising by extension from some contiguous organ or by metastasis. The chief point of predilection is the lesser curvature near the pylorus (Israel, Hansemann, Boas) and next to this the pylorus itself. In about two-thirds of the cases the growth is so situated as to cause food stagnation. About 10 per cent. of gastric cancers develop around the cardia and about 10 per cent. at some point on the anterior or posterior wall or the greater curvature. The main varieties observed are scirrhus, medullary cancer, adenocarcinoma, and squamous cell epithelioma. Transitional forms frequently occur and any variety may undergo mucoid degeneration with the production of a so-called colloid cancer.

*Scirrhus* usually affects the pylorus. It appears as a circumscribed thickening or hardening of the stomach-wall without marked prominences. Occasionally, it is very extensive and involves all the coats, converting the viscus into a shrunken rigid tube—the malignant form of the so-called "leather-bottle stomach." Scirrhous cancers grow slowly and show only a slight tendency to ulceration. Both *medullary cancer* and *adenocarcinoma* occur as soft nodules or fungous growths, which readily break down and lead to ulceration and hemorrhages. Their growth is comparatively rapid and, in the former especially, metatasis occurs early. The majority of gastric cancers are of one or the other of these two types.

[1] New York Med. Jour., April 21, 1900.

*Squamous-cell epithelioma* is relatively rare and is found almost exclusively at the cardia, usually as an extension of an esophageal cancer. *Colloid cancer* is also rare. It appears as a diffuse infiltration of the stomach-wall, or, more rarely, as a nodular mass, containing semi-transparent gelatinous material, which has been formed from the stroma and cells of the tumor through mucoid degeneration.

The effect of cancer upon the size of the stomach varies. Pyloric cancers usually result in gastrectasis, while cancers of the cardia and diffuse scirrhous growths frequently cause a reduction in the size of the organ. Distortion and displacement of the stomach often occur owing to the weight of the tumor or the contraction of perigastric adhesions.

**Symptoms.**—The disease usually begins in one of two ways: First, symptoms of gastric disturbance may develop more or less suddenly in a perfectly healthy person who never before has had more than transitory dyspepsia, and may continue for several weeks or months before their sinister import is recognized; secondly, the characteristic symptoms of cancer of the stomach may follow long-standing indigestion or a series of attacks which clearly point to chronic gastric ulcer. Occasionally, dyspeptic phenomena are absent for a long period and the patient first comes under medical supervision because of acute hematemesis, progressive weakness and emaciation, ascites, or symptoms of secondary growth in one of the other organs, usually the liver.

*The Appetite.*—As a rule, the appetite is lost early, but exceptionally it remains good during the greater part of the disease. A strong repugnance to meats and fats, while neither constant nor characteristic, is often observed.

*Pain* is absent in but a small proportion of cases. It varies in intensity from a vague feeling of discomfort to violent distress of a gnawing, burning or cramp-like character. Generally speaking, however, it is less marked than in ulcer and, though increased by eating, is not confined to the digestive period and is only temporarily relieved by vomiting. Not infrequently it is referred to the back or is transmitted upward along the sternum.

*Dysphagia* is, as a rule, an early symptom in cases of carcinoma involving the cardiac orifice.

*Vomiting* occurs at some period of the disease in the large majority of cases. It is usually, but by no means invariably, a late indication, and is especially pronounced when the pylorus is involved and there is obstructive retention. In carcinoma of the body of the stomach vomiting is sometimes absent throughout. It may occur at any period of the day, but it is most common two or three hours after meals. When there is marked ectasy of the stomach it may occur only at intervals of two or three days. The vomitus usually consists of coarse, undigested particles of food, mixed with mucus. Blood or blood pigment is also a frequent admixture. Pus is occasionally present. In pyloric obstruction with stagnation the vomitus is often profuse and has an acid (butyric acid) or putrefactive odor. When the cardia is involved there is usually regurgitation of food rather than vomiting.

*Hematemesis.*—Obvious hemorrhage from the stomach occurs in nearly one-half of the cases. As the blood often escapes slowly and remains in the stomach a sufficient length of time to undergo disintegration, the vomitus in many instances presents a brownish-black or "coffee-ground" appearance. Profuse hemorrhage is uncommon. Melena may accompany hematemesis or occur as an independent symptom. Persistent invisible hemorrhage (occult bleeding) into the gastrointestinal tract occurs in more than 80 per cent. of all cases.

*Cachexia.*—As the disease progresses cachexia supervenes with loss of

flesh and strength, the patient's general appearance frequently becoming strongly suggestive of carcinoma. The skin is pale, sallow and dry, the expression is apathetic, the features are sunken, and the muscles are wasted and flabby. Edema about the ankles and ascites are not uncommon in the late stages of the disease.

*Anemia.*—As a rule, the cachexia is accompanied by anemia of the chlorotic type, the percentage of hemoglobin being more reduced than the number of red cells. In advanced cases, especially if there has been much bleeding, the number of red corpuscles may fall as low as 2,000,000 or 1,500,000. Counts below 1,000,000 are rare. Normoblasts are often present, but megaloblasts are rarely observed. Abnormally high counts are occasionally encountered owing to the concentration of the blood from uncontrollable vomiting or deficient absorption of fluid. A moderate leucocytosis is usually noted. An absence of the normal digestion leucocytosis is a common finding, but as it is neither constant nor peculiar to cancer, it has little diagnostic significance. The anemia and cachexia are the result of subnutrition, hemorrhage, and intoxication with the products of metabolism or necrosis of the cancer cells.

*The Stools.*—Constipation, or constipation alternating with diarrhea, is present in the large majority of cases. With gastrocolic fistula the stools may be lienteric.

*The Urine.*—The urinary changes are not characteristic. The quantity of urine is usually diminished when there is marked gastrectasis or much vomiting. The excretion of nitrogen, phosphates, and indican is commonly increased, while that of chlorids is decreased. Albumin is not rarely found, and occasionally albumoses, acetone, and diacetic acid are also present.

*Jaundice, Fever, and Coma.*—Jaundice occurs in from 2 to 5 per cent. of the cases. It may be due to an extension of the malignant process to the lymph-nodes of the portal fissure, to the lesser omentum, to the pancreas, or to the liver itself. While the course of gastric cancer is for the most part afebrile, fever may arise at any time from an inflammatory complication, such as peritonitis, subphrenic abscess, or pleurisy, from an intercurrent infection, or from ulceration of the tumor itself. Fever (99°—102° F.) occurred in 43 per cent. of 472 cases analyzed by Friedenwald.[1] Coma occasionally develops as a terminal phenomenon in consequence of acidosis, or, if the liver has been invaded, from interference with the detoxifying function of that organ. Very rarely it may be due to meningeal carcinosis.

*Gastric Analysis.*—Food retention is observed in about 60 per cent. of all cases of gastric carcinoma, appearing early and becoming especially pronounced when the lesion is at or near the pylorus. Other conditions, such as gastrectasis, gastric ulcer, hypertrophic pylorus, and perigastric adhesions, may also result in the persistent retention of an appreciable amount of macroscopic food in the stomach twelve hours after a meal, nevertheless in conjunction with other signs and symptoms this finding is of considerable importance.

In about two-thirds of the cases hypochlorhydria appears early and progresses rapidly until free hydrochloric acid completely disappears from the gastric contents. The ferments also diminish and ultimately there may be persistent achylia. However, when the growth is circumscribed or develops from a peptic ulcer free acid may be demonstrated until the end of life. Inversely, achlorhydria may also occur in carcinoma of other organs, in certain anemias, in thyroid disease, as well as in certain other pathologic states of the gastric mucosa, such as chronic catarrh, atrophy, etc.

[1] Amer. Jour. Med. Sci., Nov., 1914.

This sign, therefore, is not pathognomonic of gastric cancer, and is only significant when it is persistent and occurs in association with other indications. Lactic acid is to be found sooner or later in the majority of cases. It signifies stagnation of the gastric contents and absence of free hydrochloric acid, and though not characteristic of cancer, has a certain amount of significance. In case of achlorhydria or achylia the presence of considerable amounts of soluble albumin within an hour or an hour and a half after the administration of an Ewald test-breakfast, as shown by the Wolff-Junghans' test,[1] points strongly to malignant disease if the stomach is free from protein residue when the test-meal is given and if sputum is not swallowed while the meal is in the stomach. The soluble albumin may arise from admixture of so-called "cancer juice" or from the action of a peptid-splitting ferment derived from the malignant growth.

With the occurrence of achlorhydria the long thread-like Oppler-Boas bacilli usually appear in the stomach. These acidophil organisms are non-motile, Gram positive, stain blue-red with methylene blue, and have the power of forming lactic acid from sugar. While their absence does not argue against cancer their presence in large numbers is sufficient to render a case suspicious. Sarcinæ, which are usually present in benign forms of ectasy, are not often found in the stagnating stomach-contents of carcinomatous cases, as lactic-acid fermentation is inimical to their growth.

In addition to the Oppler-Boas bacilli, the gastric contents may show microscopically yeast cells, red corpuscles, leuycocytes, and pus cells. In the later stages, after ulceration has set in, bits of tumor are occasionally seen, and are, of course, positive evidence of cancer.

Invisible traces of blood (occult blood) are present in the gastric residuum or feces in the vast majority of cases, and their persistent absence is strong evidence against the disease. They are found also in peptic ulcer, but less constantly. A blood test of the stools is often positive when that of the gastric filtrate is negative. For the tests to be reliable no meat, raw vegetables (chlorophyll) or drugs should be taken for two or three days beforehand and other sources of blood (epistaxis, gingivitis, hemorrhoids, anal fissure, passive congestion of the stomach from cirrhosis of the liver or cardiac insufficiency, catamenia etc.) should be carefully excluded. If the benzidin test is negative it may be concluded that no blood is present, but if it is positive the result should be controlled by the guaiac or aloin test.

**Physical Signs.**—If the process is well advanced inspection may reveal abnormal fullness in the epigastrium, a diffuse area of aortic pulsation, peristaltic or antiperistaltic waves, a circumscribed protrusion corresponding to the tumor, and occasionally the entire outline of the stomach, if the organ is much distended and the abdominal wall is thin and relaxed. Palpation serves to detect sooner or later in the majority of cases a hard mass within the abdomen. Tumors of the anterior wall and of the pylorus are the most readily recognized, while those of the cardia, lesser curvature, and posterior wall often remain inaccessible to palpation during the entire life of the patient. Even when no definite mass can be felt, localized rigidity or "stiffening" of the abdominal wall may often be observed, especially when the pylorus is obstructed. The location of perceptible tumors varies with the part of the stomach affected, and with size and position of the viscus. They usually occupy the epigastrium or the right hypochondrium, but may be found in almost any part of the abdomen. Unless adherent to adjacent structures,

[1] Wolff and Junghans, Berlin klin. Woch., 1911, xlviii, 978; Clarke and Rehfuss, Jour. Amer. Med Assoc., 1915, lxiv, 1737; Friedenwald and Kieffer, Amer. Jour. Med. Sci., 1916, clii, 321.

they are usually movable on manipulation and on rotation of the body from side to side. They may also move to some extent with respiration, although respiratory movability usually implies adherence to the liver.

X-ray findings, especially screen-observations, when interpreted by an expert roentgenologist, afford valuable information in many instances, but like other methods of investigation, they often fail in the early stages of the disease. The most important roentgen signs are filling-defects, due to the projection of the tumor into the lumen of the stomach, and pyloric obstruction with delayed emptying of the stomach, as shown by a six-hour residue in the stomach after a meal containing opaque salts, or, less frequently, gaping of the pylorus with rapid emptying, owing to rigidity of the pyloric ring.

*Superficial Metastases.*—Enlargement of the lymph-nodes in the left supraclavicular region near the termination of the thoracic duct, to which Virchow first drew attention, has some diagnostic significance, but it is only occasionally observed and is not absolutely pathognomonic. Secondary carcinoma of the umbilicus, with induration and protrusion of the umbilical ring, is sometimes noted, particularly in women. Boas,[1] observed it in 3 of 141 cases. Schnitzler, Palmer, Boas, Turner and others have pointed out the frequency with which metastatic deposits may be felt in the anterior wall of the rectum, 3 or 4 inches from the anus, even when there are no symptoms suggestive of their presence.

**Complications.**—The most common complications are those arising from *extension of the malignant process beyond the stomach.* This may occur through continuity of structure, through adhesions, through the lymphatics, or more rarely through the veins, especially the portal vein. The lymph-nodes most frequently involved are the perigastric nodes, those at the hilum of the liver, those around the cœliac axis, the superior mesenteric nodes, the mesocolic nodes and the lumbar nodes. The organs most frequently affected are the liver, intestines, pancreas and lungs. Extension to the peritoneum and omentum is also common. Invasion of the spine is occasionally observed. Metastatic growths in the liver are found in from 25 to 30 per cent. of the cases. Metastases are rare in the brain (none in Kaufmann's 227 cases, none in Friedenwald's 672 cases, and 1 in Mielecki's 156 cases), and the muscles are almost exempt. As the tumor grows ulceration is likely to occur and lead to *inflammation* (*adhesive* or *suppurative*) *of adjacent structures*, such as the peritoneum, pleura, lung, etc. Occasionally (3 to 5 per cent. of the cases) ulceration results in *perforation* into the peritoneum, with acute peritonitis or localized abscess, into the pleura or pericardium, or even externally through the abdominal wall. One-half of Zweig's,[2] collected cases of *gastrocolic fistula* were due to gastric cancer. The most constant symptoms of this complication are fecal vomiting, severe diarrhea with lienteric stools, excessive thirst and rapid emaciation.

*Ascites* sometimes appears in the advanced stages of the disease, owing to invasion of the peritoneum, portal obstruction, or intense anemia. Occasionally a *thrombus* develops in the femoral vein causing edema of one extremity or in the portal vein causing ascites, enlargement of the spleen, and gastro-intestinal hemorrhage. *Tetany* has been observed in a few instances and so also has *polyneuritis.*

**Diagnosis.**—In the early stages, when tumor, hematemesis and cachexia are wanting the diagnosis is often impossible without an exploratory operation. Even the x-ray commonly fails to reveal the growth while it is still in the operable stage. Gastric cancer should be suspected, however, when indiges-

[1] Archiv. f. Verdauungskrank., 1901, vii.
[2] Wien. klin. Rundschau, 1900.

tion first appears after the age of 40 and proves resistant to ordinary dietetic and medicinal treatment. If in addition, the motility of the stomach is impaired, if free hydrochloric acid is constantly absent from the gastric contents, and if occult blood persistently appears in the feces, the diagnosis of cancer is much strengthened.

In *chronic gastritis* the course is less rapid and marked by remissions, there is little emaciation and no cachexia, vomiting is less constant, hematemesis and occult bleeding are exceptional, the secretion of hydrochloric acid is less frequently suppressed, lactic acid and Oppler-Boas bacilli are not usually found in the gastric contents, the motor power of the stomach is not much affected, no tumor can be detected on palpation, and the x-ray appearances are negative.

In certain cases it is difficult to differentiate *peptic ulcer* from gastric cancer. Both conditions are likely to cause pain, vomiting and hematemesis, and, moreover, cancer frequently develops on the basis of ulcer, and occasionally an ulcer is productive of palpable swelling or induration. However, in simple ulcer, as a rule, the age of the patient argues against cancer, emaciation and cachexia are absent or are very late phenomena, pain is more closely confined to the digestive period, vomiting occurs at the height of the pain, is easier, and gives more relief than in cancer, hemorrhage is more profuse, and the vomited blood less changed in appearance, occult bleeding is less constant and more likely to be checked by rest and protective dieting, the secretion of hydrochloric acid is increased or normal rather than suppressed while lactic acid fermentation is wanting, and the x-ray shows a crater projecting *from* the gastric lumen (niche), with an indentation (incisura) opposite, or, in the case of duodenal ulcer, marked deformity of the bulb, instead of a permanent filling-defect arising from the projection of a tumor *into* the lumen of the stomach.

The diagnosis of *cirrhosis of the stomach* (linitis plastica) from the diffuse form of scirrhous cancer is rarely possible. *Cancer of the transverse colon*, of the *gall-bladder* or of the *pancreas* may closely resemble cancer of the stomach, but information afforded by palpation, especially after inflation of the stomach, by x-rays, and by analysis of the gastric contents will usually prevent an error in diagnosis. Rapid emaciation, severe epigastric pain, progressively increasing jaundice with enlargement of the gall-bladder and signs of impaired pancreatic function are additional evidences of pancreatic involvement.

*Pernicious anemia* sometimes gives rise to confusion, but in this disease emaciation is often absent, marked remissions frequently occur, the red-cell count is usually less than 2,000,000, the color index of the blood is high, the leucocyte count is low, macroblasts can generally be found, hematemesis is rarely noted and the x-ray appearances are negative.

**Course.**—The outlook is extremely grave. Medical treatment offers no hope of permanent relief and surgical intervention is completely successful in but a small proportion of cases. The duration of the disease, estimated from the time the first symptoms appear, varies from 2 or 3 months in the "fulminant" type to several years in the usual form. It averages about one year. Generally speaking, it is longer with hard cancers and those affecting the body of the stomach than with soft cancers and those affecting the orifices. Temporary improvement with a gain in weight, occasionally amounting to ten pounds or more, is not uncommon, and when observed late in the disease is probably due to partial disintegration of the tumor. Death may result from inanition, metastases, intercurrent infection, or, more rarely, from perforation, hemorrhage or acute intoxication (coma).

**Treatment.**—An exploratory operation is advisable in persons past 40 in whom pronounced digestive disturbances arise without obvious cause and persist despite an appropriate diet and medical treatment, especially if hypochlorhydria or achlorhydria, food retention, occult bleeding or abnormality of the gastric contour, as shown by x-ray, are among the manifestations. Pylorectomy or partial gastrectomy offers hope of a considerable prolongation of life and even of an actual cure when done at an early stage of the disease. Removal of the cancer-bearing area, however, is contraindicated when there is evidence of metastasis to any of the accessible lymph nodes, as those above the left clavicle, at the umbilicus or in the rectal shelf or to any of the other organs, or when there are signs of free fluid in the peritoneum. The presence of a palpable tumor is not in itself a sign of inoperability, especially if it is movable. In cases of irremovable cancer a palliative operation, such as gastro-enterostomy, gastrostomy or jejunostomy, may be done to relieve distress and to prolong life for a few months. Seven hundred and thirty-six resections were done at the Mayo clinic[1] with a mortality of 13.7 per cent., 746 explorations, with a mortality 2.9 per cent. and 612 palliative operations with a mortality of 11.1 per cent. Of patients who survived resection, 38.6 per cent. were free from recurrence for 3 years or more after operation and 26 per cent. for 5 years or more after operation.[2]

*Medical Treatment.*—In the early stages of the disease, if the pylorus is still patulous, a mixed diet of readily digested food is often well borne. Later, when there is retention, food should be selected that will make small demands on the stomach and that will leave little residue. Bitters—calumba, nux vomica, gentian—are sometimes employed with advantage. In many cases hydrochloric acid and pepsin are useful. Lavage affords the best means of relieving the distressing symptoms that result from retention. Vomiting not dependent upon retention may be treated with such remedies as carbonated water, bismuth subnitrate, cerium oxalate and hydrocyanic acid. In refractory cases rectal feeding may be required for a time. Acid eructations and flatulency are sometimes relieved by antacids and antiseptics, but, as a rule, lavage is more effective. Severe pain will require opium, local sedatives, such as hydrocyanic acid, cocain, and chloroform and hot applications.

## SARCOMA OF THE STOMACH

Sarcoma of the stomach is rare, occurring in about 1 per cent. of the cases of gastric malignancy. Douglass[3] in 1920, reported 3 cases and analyzed 230 from the literature. The disease may develop at any period of life, but it is found in young adults much more frequently than carcinoma. The two sexes are about equally affected. The tumor, which in the vast majority of cases is primary, may be of any type, may be nodular or diffuse, and may be located in any part of the stomach. Lymphosarcoma and round cell sarcoma are the most common forms and the region of the pylorus is the favorite site, although other parts of the stomach are much more frequently affected than in carcinoma. Even when the pylorus is involved, pronounced stenosis is not often observed. Occasionally, the growth reaches an enormous size, as in Salomon's[4] case, in which it weighed 14 pounds. The

[1] Ann. of Surg., 1919, lxx, 237.
[2] Surg., Gyn. and Obstet., April, 1918.
[3] Annals of Surgery, May, 1920.
[4] Trans. Path. Soc., London, 1914, lv.

process spreads by continuity of structure and by metastasis, the latter being by way of the bloodvessels. The clinical picture resembles that of carcinoma of the stomach, but the gastric symptoms are, as a rule, less severe. The diagnosis cannot be made with certainty. The only hope of cure lies in surgical treatment, and this is advisable in the absence of metastasis. In a few instances the results of operation have been entirely satisfactory. With palliative treatment the average duration is about one year.

## CIRRHOSIS OF THE STOMACH

(Linitis Plastica; Leather-bottle Stomach)

These terms are applied to marked thickening of the wall of the stomach, due chiefly to an extensive overgrowth of fibrous tissue in the submucosa and to secondary hypertrophy of the muscularis. The resemblance of the interlacing bands of connective tissue to woven linen, suggested to Brinton[1] the name "linitis." Two forms of the process are recognized—the localized, which shows a predilection for the pylorus and which is comparatively rare, and the diffuse. In the latter the stomach is considerably reduced in size and its wall is thick and rigid (leather-bottle). The mucous membrane may be intact throughout or it may present large or small areas of ulceration. The condition in the majority of cases is one of infiltrating scirrhous carcinoma, but occasionally it appears to be a result of simple inflammation, of syphilis, or of hyperplastic tuberculosis. According to Lyle's[2] statistics the disease affects men much more frequently than women and the greatest number of cases occur between the ages of 40 and 60 years. The symptoms closely resemble those of scirrhous carcinoma of the stomach, but the lesion may be clearly recognized by roentgen examination. Even at operation, however, it may be impossible to determine whether the fibrosis is benign or malignant. In a few instances gastro-enterostomy has resulted in a clinical cure.

## STENOSIS OF THE PYLORUS IN INFANTS

(Hypertrophic Pyloric Stenosis)

Stenosis of the pylorus is not uncommon in infants and is probably congenital. It may be due to muscular spasm, to hypertrophy of the pyloric wall, or to a combination of both of these conditions. Cases of the combined type are the most numerous. Whether the hypertrophy is a primary congenital defect and the spasm secondary, as Hirschsprung[3] maintained, or the spasm is primary and a result of gastric irritation or nervous disturbances, as John Thomson[4] believed, is still undetermined. The disease usually shows itself within the first two or three weeks of life and rarely appears after the second month. Males are affected much more frequently than females.

**Symptoms.**—Vomiting is the first symptom. It may occur after each feeding or only after every two or three feedings. In the latter event it is

[1] Brinton, W.: Diseases of the Stomach, London, 1854.
[2] Annals of Surgery, Nov., 1911.
[3] Jahrb. f. Kinderheilk., 1888, xxviii, 61.
[4] Pfaundler and Schlossmann, Handbuch der Kinderheilk, 1906, ii.

likely to be forcible and of a projectile character, and the ejected material to be comparatively large in amount. With the occurrence of secondary dilatation of the stomach milk is often found in the viscus after a three-hour interval. As a result of the frequent vomiting, the infant is persistently hungry, emaciation occurs more or less rapidly, and constipation becomes pronounced, the stools that are passed sometimes consisting solely of mucus and bile. When the stomach is partly filled, inspection of the epigastric region almost always reveals perstaltic waves passing from left to right, and deep palpation, a small, hard, movable tumor, two or three centimeters long, to the right and above the navel. Roentgen examination, while sometimes misleading, may be of considerable value in diagnosis.

The **diagnosis** of pyloric stenosis in infants is usually not difficult, if the possible existence of the condition is kept in mind and the patient is carefully examined. The chief danger lies in concluding too hastily that the vomiting is due merely to an ordinary digestive disturbance. Congenital atresia of the duodenum, of which there are about 100 cases on record (Cantley[1]), produces a clinical picture similar to that of hypertrophic stenosis of the pylorus, but in the former vomiting often continues even when food is withheld, the ejected material is almost always bilious, and death usually occurs in a very few days. It is not often possible to distinguish positively between the spasmodic and the hypertrophic types of stenosis. However, in pylorospasm the vomiting, as a rule, occurs less frequently and is less forcible, the stools are likely to remain more or less fecal, the body-weight is better maintained and a pyloric tumor cannot be felt.

**Treatment.**—Medical treatment sometimes succeeds when the stenosis is entirely or mainly spasmodic, but in the majority of all cases operation is required. Medical treatment consists in using breast-milk, or, if this is not available, a dilute mixture of cow's milk low in fat and sugar, in small quantities at frequent intervals, in washing out the stomach once or twice a day with a solution of sodium bicarbonate (2 per cent.), and in administering normal saline solution by the rectum or by subcutaneous injection. Drugs are of somewhat doubtful value, but sedatives, especially bromids and belladonna, sometimes seem to be of service. If definite improvement does not occur within a week or ten days, or if wasting is already pronounced recourse should be had to surgical treatment. The Fredet-Rammstedt[2] operation has apparently yielded the best results and can be performed by a skillful surgeon within 20 minutes. It consists in incising longitudinally the serous and muscular layers of the pylorus, but not the mucous layer, and leaving the wound in the stomach unsutured. The mortality-rate is much higher in artificially-fed babies than in breast-fed babies, and increases in direct proportion to the amount of weight lost previous to operation (Goldbloom and Spence[3]). Downes[4] reports 165 operations with 30 deaths (17.1 per cent.). The mortality among patients coming to operation within 4 weeks from the onset was less than 8 per cent. Ladd[5] reports 78 pyloroplasties with a mortality of 7.6 per cent. Feeding by the mouth may be begun two hours after operation, but at first only 2 or 3 drams of milk (preferably breast-milk from a bottle) should be given every 2 or 3 hours.

[1] British Jour. Children's Diseases, April–June, 1919.
[2] Fredet, Rev. de chir., 1908, xxxvii, 208; Rammstedt, Med. Klinik., 1912, viii, 1702.
[3] Amer. Jour. Dis. Children, April, 1920.
[4] Jour. Amer. Med. Assoc., July 24, 1920.
[5] Surg. Clin. North Amer., June, 1921.

## ACUTE GASTRECTASIS

(Acute Dilatation of the Stomach)

Acute dilatation of the stomach is comparatively rare, although it is probably more common than is generally supposed. About three-fourths of the cases have been in young adults. A large number have followed surgical operation, especially upon the abdominal organs. In another comparatively large series of cases the symptoms have suddenly developed after overloading of the stomach. In some instances trauma has been a factor. Many cases have occurred in the course of or during convalescence from acute infectious diseases, notably pneumonia or typhoid fever. Occasionally, a chronic wasting disease has been assigned as a direct or contributing cause. In 6 of the 102 cases analyzed by Conner[1] there was deformity of the spine.

The pathogenesis of the disease is not definitely known. The theory of acute neuroparesis probably has the most adherents. Kinking of the duodenum or constriction of the duodenum by a tense mesentery has been found in a number of cases, but whether this has been the cause or an effect of the gastrectasis is uncertain. Kelling[2] attributes the condition to simultaneous closure of the cardia and pylorus. The chief feature of the post-mortem picture is the enormous size of the stomach. In about one-half of the cases the duodenum is also dilated, and occasionally even the jejunum is involved.

**Symptoms.**—Clinically the disease is characterized by more or less pain and tenderness in the epigastrium, uncontrollable vomiting of large quantities of foul smelling, bile-stained fluid, great thirst, constipation (diarrhea in a few cases), abdominal distention, especially pronounced in the epigastrium and disappearing after lavage, the occurrence of splashing sounds below the level of the umbilicus, and, in severe cases, the rapid development of collapse. In individual cases, any of these symptoms, even the vomiting, may be wanting. By means of the stomach-tube large quantities of fluid, sometimes several pints, may be withdrawn from the stomach with immediate relief of symptoms. The vomit, although foul, is rarely fecal; the temperature, unless the gastectasis has occurred in the course of a febrile disease, is normal or sub-normal; muscular rigidity is absent in the vast majority of cases, and so also is visible peristalsis.

The *duration* of the disease in fatal cases has varied from a few hours to two weeks and has averaged from 3 to 5 days. In favorable cases several weeks may elapse before recovery is complete. The prognosis is grave unless appropriate treatment is instituted at once. In 217 cases collected by Laffer,[3] the mortality was 63.5. In **diagnosis** postanesthetic vomiting, intestinal obstruction, perforative peritonitis, acute pancreatitis, and uremia are all to be considered. Of especial value in differentiation are the quantity and character of the vomit, the objective signs, and the results of lavage.

**Treatment.**—This consists in thoroughly washing out the stomach with warm saline solution, even if the patient seems moribund, elevating the foot of the bed, maintaining the right or left antero-lateral abdominal position, or if the patient's strength permits, the knee-chest position, withholding all food and drink by the mouth, using saline enemas to combat thirst and collapse, and administering subcutaneously such muscle stimulants as physostigmin sulphate—$\frac{1}{50}$ grain (0.0013 gm.)—solution of the pituitary body—15 minims (1.0 mil)—and strychnin sulphate —$\frac{1}{30}$ grain (0.002 gm.).

[1] Amer. Jour. Med. Sci., Mar., 1907.
[2] Archiv. f. klin. Chir., 1901, lxiv.
[3] Annals of Surgery, April, 1908.

## CHRONIC GASTRECTASIS

(Chronic Dilatation of the Stomach)

**Definition.**—The term gastrectasis is applied to an increase in the capacity of the stomach with deficiency, either actual or relative, in its expulsive power. Increased capacity alone (megalogastrica) does not constitute gastrectasis, at least in the clinical sense. There may be enlargement of the stomach without abnormal retention of ingesta, and, on the other hand, there may be pronounced motor insufficiency without any increase in the size of the organ. Nevertheless, retention of food, whatever its cause, always favors the occurrence of gastrectasis. Two forms of chronic dilatation of the stomach are recognized, the obstructive and the non-obstructive.

**Etiology.**—*Obstructive gastrectasis* is due to an obstruction at or near the pylorus, its chief causes being (1) a tumor (usually carcinoma) of the stomach itself or of an adjacent organ; (2) a cicatrix following the healing of a peptic ulcer; (3) inflammatory adhesions about the pylorus or duodenum; and (4) persistent pylorospasm from ulcer, gastric erosion, or a more remote lesion, such as chronic cholecystitis, appendicitis, etc.

*Non-obstructive gastrectasis*, the less common form of the disease. may result from habitual intemperance in eating and drinking; it may occur in the course of chronic disease attended by general malnutrition; it may be the sequel of some other disease of the stomach, notably chronic gastritis; and occasionally it seems to depend upon a congenital weakness of the gastric muscle. Many cases of gastrectasis that appear to be non-obstructive are probably in reality obstructive, for undoubtedly abnormal distention of the stomach may result from a spasmodic stenosis of the pylorus of which there may be no anatomical evidence at either operation or necropsy.

**Morbid Anatomy.**—All degrees of dilatation are observed. The largest stomachs occur in stenosis of the pylorus. There are cases on record in which the organ has seemed to fill nearly the whole abdominal cavity and has attained a capacity of 10 or more liters. In the non-obstructive form the stomach is distended chiefly at its lower pole and the gastric wall is usually thin and atrophic; in the obstructive form the stomach is enlarged throughout and the gastric wall is often thickened, especially in the region of the pylorus, in consequence of muscular hypertrophy. In long-standing cases, however, microscopic examination usually reveals atrophy and degenerative changes in the muscle-fibers.

**Symptoms.**—These vary with the cause and degree of the dilatation. Slight degrees of ectasy, especially of the non-obstructive form, often exist without producing any symptoms whatever. In pronounced cases the chief symptoms are an uncomfortable sensation of fulness after the meals, frequent belching and eructations, vomiting of large amounts of sour fluid and partially digested food at relatively long intervals after eating, increased thirst, obstinate constipation, decreased secretion of urine, dryness of the skin and mucous membranes, and more or less emaciation. Various nervous phenomena, such as headache, dizziness, and mental depression, are sometimes noted, and are probably due to auto-intoxication. In rare instances tetany develops. Symptoms referable to the primary cause of the dilatation, such as those of peptic ulcer or of pyloric carcinoma, are also present in many cases.

Vomiting is frequently absent in non-obstructive gastrectasis, but it is always an important symptom in ectasy due to pyloric stenosis. It occurs several hours after the food is taken, sometimes only at intervals of two or three days, and is usually profuse, the patient himself not infrequently expressing

the opinion that he vomits more than he eats or drinks. The vomited matter is sour, of a dirty gray or brownish color, and on standing separates into three layers, froth on top, turbid fluid in the middle, and a sediment of undigested food at the bottom. Not rarely it contains remnants of food that was eaten 24 or 48 hours before. The acid content varies. Organic acids introduced with the food and resulting from fermentation are often abundant. Hydrochloric acidity may be high, especially in benign stenosis, while achlorhydria with lactic-acid fermentation is the rule in malignant cases. Yeast cells are likely to be present in all forms of ectasy, but sarcinæ are usually absent in carcinoma, the achlorhydria of the latter being inimical to their growth while favoring that of the Oppler-Boas bacilli. The thirst, scanty urine, and dryness of the tissues are to be ascribed to the small quantity of fluid passing through the pylorus into the intestine where absorption occurs.

*Physical Signs.*—The abdomen may be unduly prominent, and in thin subjects with pyloric stenosis the entire outline of the stomach may be visible, the greater curvature appearing some distance below the navel. In obstructive cases peristaltic waves may sometimes be seen, especially after gentle manipulation of the abdominal wall, and less frequently intermittent hardening of the stomach ("stomach stiffening") may be detected on palpation. Splashing sounds over the stomach are evidence of stasis only when they can be heard in the morning before breakfast or seven hours or more after an ordinary meal. Percussion as a means of determining the size of the stomach is of comparatively little value, even if practised after the organ has been inflated through the stomach-tube, and at present is not often employed. The use of the stomach-tube to determine the quantity of residue in the stomach at a certain time after the ingestion of a test-meal frequently yields important information. The recovery of some remnants of food 7 or 8 hours after a Riegel test-meal (see p. 412) is indicative of motor insufficiency, but it does not signify necessarily pyloric stenosis or even atonic dilatation of the stomach. Persistent and pronounced twelve-hour retention, however, is always strong evidence of an organic lesion at or near the pylorus. In non-obstructive gastrectasis food is rarely found in the stomach after the twelve-hour period. By far the best method of determining the exact size of the stomach is examination with the roentgen-ray after a meal containing an opaque salt, such as barium sulphate or bismuth subcarbonate.

**Diagnosis.**—The recognition of gastrectasis is, as a rule, comparatively easy. The form of the disease is usually revealed at once by the x-ray, and in many cases it is perfectly obvious from the symptoms alone. Recurrent vomiting of large amounts of fluid, visible or palpable peristalsis, the presence of tumor, and the finding of an appreciable quantity of food in the stomach 12 hours or longer after an ordinary meal are almost certain indications of organic obstruction at the pyloric region.

**Prognosis.**—The prognosis of chronic dilatation of the stomach must always be guarded until the nature of the primary disease is disclosed. Non-obstructive dilatation, even if somewhat pronounced, is amenable to cure, provided it has not lasted too long and the underlying cause is one that can be removed. In obstructive dilatation from causes other than carcinoma surgical intervention holds out much hope of permanent improvement or even of actual cure.

**Treatment.**—The food should be nutritious, concentrated, and readily digestible, and should be taken in small amounts at somewhat frequent intervals. Liquids are best taken when the stomach is empty and then only in moderate quantities. The importance of thorough mastication must be

emphasized. Rest in the recumbent position for an hour after each meal, especially if the patient lies on the right side, favors rapid evacuation of the stomach. A carefully adjusted abdominal bandage affords comfort and gives mechanical support to the stomach. If there is any appreciable stagnation of food lavage should be practised daily, preferably in the early morning or late evening. In mild cases lavage is usually unnecessary. In the non-obstructive form systematic exercise in the open air, hydrotherapy, and abdominal massage, if skillfully applied, are valuable aids. Electricity is of little or no value.

Medicinal treatment must be adapted to the condition with which the motor insufficiency is associated, as, for instance, chronic gastritis, general malnutrition, etc. In uncomplicated cases of simple atonic dilatation nux vomica is useful. It should be given in the form of the tincture, three times a day and in doses gradually increased to 30 minims (2.0 mils). Antiseptics, such as creosote and betanapthol, are sometimes of service in lessening the gaseous eructations and the sense of pressure within the stomach arising from fermentation, but, as a rule, more relief is afforded by lavage. The following combination suggested by the late Dr. John H. Musser is often useful:

℞. Creosoti ..... ♏xii (0.8 mil)
Spiritus ammoniæ aromatici ..... f℥ii (8.0 mils)
Spiritus chloroformi ..... f℥i (4.0 mils)
Sodii bicarbonatis ..... ℥ii (8.0 gm.)
Aquæ menthæ piperitæ ..... q. s. ad f℥iii (90.0 mils) M.
Sig.—A teaspoonful in a wineglassful of water half an hour after meals and at bedtime.

Constipation is, as a rule, best treated by simple enemas or by suppositories. In some cases, however, Rochelle salt in small doses or mild vegetable cathartics may be employed with advantage.

In obstructive dilatation recourse should be had to surgical treatment, gastroenterostomy, pylorectomy, or pyloroplasty being indicated according to the condition presented.

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## HEMATEMESIS

Vomited blood may be derived from sources other than the stomach. Thus, blood from the nose, mouth or throat, from the esophagus, or from the lungs may be swallowed and later ejected from the stomach. On the other hand, hematemesis is not rarely absent in cases of gastric hemorrhage, the blood escaping from the stomach by way of the intestines. True gastric hemorrhage (gastrorrhagia) is most frequently the result of (1) peptic ulceration of the stomach or duodenum, (2) carcinoma of the stomach, (3) cirrhosis of the liver, (4) splenic anemia or some other obscure form of splenomegaly, (5) acute gastritis arising from the action of corrosive poisons or other irritants, or (6) trauma, the injury being external or direct by foreign bodies. Hemorrhage occurs in about 25 per cent. of the cases of peptic ulcer and is often profuse. It occurs at one time or another in about 50 per cent. of the cases of gastric carcinoma, and in this disease it is usually slight and recurrent, the blood forming the so-called "coffee ground" vomitus. In cirrhosis of the liver the bleeding is often, but not invariably, caused by the rupture of esophageal varices and is usually profuse. Only 6 per cent. of 60 cases of fatal hemorrhage due to cirrhosis of the liver analyzed by

Preble[1] showed the ordinary clinical evidences of the disease. In so-called primary splenomegaly with anemia bleeding from the stomach may be of great severity and may occur over many years.

Much less frequently gastrorrhagia is due to (7) venous stasis in the stomach from decompensated lesions of the heart or compression of the lower vena cava by tumors, to (8) constitutional diseases which bring about a blood dyscrasia through infection or intoxication or otherwise, such as the specific fevers, pernicious anemia, scurvy, leukemia, purpura, hemophilia, or to (9) gross lesions of the stomach other than peptic ulcer, carcinoma and acute gastritis, such as syphilis, tuberclosis, sarcoma and multiple erosions of unknown origin. Hematemesis may also be a conspicuous symptom in (10) acute pancreatitis and (11) in mesenteric embolism or thrombosis. It sometimes occurs as a result (12) of focal infection within the abdominal cavity. Eusterman[2] found that about 2 per cent. of the cases of appendicitis and about 5 of the cases of cholecystitis gave a history of previous bleeding. Hutchison[3] records 24 cases of fatal hemorrhage from the stomach after operations of various kinds upon the abdominal viscera, but chiefly after appendectomy. The bleeding in these cases is usually ascribed to erosions or acute ulcers resulting from thrombi or emboli of septic origin. According to Pringle,[4] who has observed 16 fatal cases, the lesion is often in the esophagus. Gallard, Boas, Welch and Buday[5] have reported cases of profuse hematemesis from (13) the rupture of sclerotic arteries or miliary aneurysms in the stomach and Stadelmann[6] has shown that obscure bleeding from the stomach may arise (14) from the rupture of idiopathic varicose veins beneath the gastric mucosa. Fisher[7] reports 4 cases of gastrorrhagia (15) associated with chronic nephritis (toxemia). Finally, in a certain number of cases of profuse hemorrhage from the stomach no lesion is discoverable at operation or at necropsy. W. Hale White[8] has suggested that such hemorrhages may be due to oozing of blood (gastrostaxis) in consequence of an injury to the vessels by an endothelial toxin. Moynihan, Bolton[9] and others, however, discredit this view and believe that this form of bleeding is always dependent upon minute fissures or erosions. In some of the cases the condition is clinically indistinguishable from peptic ulcer.

**Symptoms.**—The quantity of blood that is vomited varies from mere specks or streaks to a liter or more. A part of the blood usually passes into the intestines. Hemorrhage so slight that the blood can be detected only by chemical tests or by means of the microscope is referred to as occult bleeding. The appearance of the blood also varies. If the hemorrhage is profuse and the stomach empties itself almost at once the blood presents its usual characteristics. Some of it may be clotted, although the bulk of it is likely to be fluid. On the other hand, if the hemorrhage is small the blood may remain in the stomach for a long time and when eventually ejected appear as brownish-red masses or dark granular particles resembling coffee-grounds. After large hemorrhages the stools frequently acquire a tarry appearance and become very offensive. Small hemorrhages have no influence on the general condition of the patient, but large ones, especially if

[1] Amer. Jour. Med. Sci., Mar., 1900.
[2] St. Paul Med. Jour., 1913, xx.
[3] Proc. Royal Soc. Med., 1911, vol. iv, No. 3.
[4] Jour. Path. and Bact., Edinburgh, Oct., 1921.
[5] Ziegler's Beit., 1908, xliv, 327.
[6] Berlin klin. Woch., May 5, 1913.
[7] Bristol Med.-Chir. Jour., 1904, xii, 234.
[8] Lancet, Nov. 3, 1906; Lancet, Feb. 17, 1912.
[9] Brit. Med. Jour., May 21, 1910.

repeated at short intervals, produce the symptoms of acute anemia, namely, pallor of the skin and mucous membranes, weakness, ringing in the ears, dizziness, blurring of vision, tendency to syncope, etc. A moderate rise of temperature and transient mild delirium may also occur.

The **diagnosis** of gastric hemorrhage is, as a rule, easy. Material resembling blood in the ejecta, such as chocolate, red wine, and colored medicines, are not likely to cause confusion, if due care be exercised. Bleeding from the nose, mouth, or esophagus may usually be excluded by the history of the case, the course of the illness, and a thorough physical examination of the patient. Occasionally, difficulty is experienced in distinguishing between hematemesis and *hemoptysis*. However, in hematemesis the vomiting is often preceded by a sense of fulness or of warmth in the epigastrium, the blood is usually dark in color, of an acid reaction, and mixed with particles of food, and the associated symptoms and signs point to disease of the stomach itself or one of the other abdominal organs; in hemoptysis, on the other hand, tickling in the throat or coughing commonly precedes the hemorrhage and vomiting, if it occurs at all, comes later, the blood is usually light in color, alkaline in reaction, foamy and mixed with mucus or muco-pus, and the associated symptoms and signs point to pulmonary or cardiac disease. The sudden occurrence of pallor and weakness without obvious cause in patients with gastric symptoms should always lead to a careful inspection of the stools, for not rarely in gastric hemorrhage the blood escapes into the bowel instead of being vomited.

**Prognosis.**—Hematemesis, even if severe, does not often endanger the life of the patient. It has been shown that a vigorous person may survive after losing rapidly as much as 3 liters of blood (Gjestland[1]). Nevertheless, profuse hemorrhages, such as sometimes occur in peptic ulcer, cirrhosis of the liver, and splenomegaly, occasionally prove fatal, and even small hemorrhages are important, because there is always danger of a recurrence.

**Treatment.**—In the treatment of hematemesis absolute rest is essential. No food of any kind should be given by the mouth. The foot of the bed should be elevated and an ice-bag applied over the stomach. A small dose of morphin may be given hypodermically to lessen restlessness and anxiety, although its use has been objected to on the ground that it tends to relax the gastric muscle. The solution of epinephrin (1:1000), in doses of 1 dram (4.0 mils), in a wineglassful of water, every 20 minutes or half hour, may prove useful. Lavage with ice-water or with hot water (120° F.) has apparently been of benefit in some cases.

The passage of the stomach tube is, however, absolutely contraindicated if there is any evidence of hepatic cirrhosis, as the latter often gives rise to extensive varices in the esophageal wall. In persistent bleeding coagulin (a derivative of blood-platelets) is worthy of trial. From ½ to 1 ounce (15–30 mils) of a 10 per cent. solution may be given by the mouth. Surgical intervention is rarely indicated during the course of severe gastric hemorrhage. Operation is advisable, however, in recurring profuse hemorrhages, especially if the bleeding is definitely associated with peptic ulcer or splenomegaly (splenectomy).

Collapse following hematemesis will call for elevation of the foot of the bed, hot applications, bandaging of the legs and arms, subcutaneous or intravenous injections of warm saline solution, and above all, if feasible, transfusion of blood.

[1] Norsk. Mag. f. Laegevidenskaben, 1913, 122.

# DISEASES OF THE INTESTINES

## DIARRHEA

**Definition.**—The term diarrhea implies abnormal frequency and fluidity of the intestinal evacuations.

**Etiology.**—The increased fluidity of the feces, which is an inseparable condition, may be primary and depend upon an abnormal transudation or exudation of water from the intestinal wall into the lumen of the bowel, or it may be secondary, the result of increased peristalsis and a consequent interference with the absorption of water in the small intestine. The causes producing diarrhea may operate through the bowel itself, through the intestinal contents, through the blood, through the nervous system, or through two or more of these channels conjointly. For clinical purposes the forms of diarrhea may be classified as follows:

**Diarrhea of Intestinal Origin.**—Water in excess, various articles of diet, such as fats, oils, fruits and coarse vegetables, and even overeating itself may excite diarrhea without causing any organic changes in the bowel, this effect being purely mechanical or due to indigestion and the formation of irritant products which excite peristalsis. Cathartics cause frequent liquid stools either by directly stimulating peristalsis, as in the case of the vegetable drugs, or by increasing the amount of fluid in the intestines, as in the case of the salines. In persistent constipation intercurrent attacks of diarrhea (stercoral diarrhea) sometimes occur, owing to irritation of the intestines by the retained ecal matter. Similarly, collections of intestinal parasites may set up diarrhea. . Finally, in various organic diseases of the bowel, such as catarrhal inflammation (enteritis), ulceration and malignant growth, diarrhea is an important symptom.

**Diarrhea in Diseases of Digestive Organs Other Than the Bowel.**—Certain disorders of the stomach, particularly achylia, insufficiency of the pylorus, and hypersecretion with high acidity, are not rarely associated with persistent diarrhea. In the first two conditions the food being insufficiently prepared for intestinal indigestion probably acts directly as an irritant or undergoes putrefactive changes in the bowel resulting in the production of irritant substances. In the case of hypersecretion it is likely that the acidity of the chyme is sufficient in itself to excite increased peristalsis. It is important to recognize that in gastrogenic diarrhea symptoms referable to the stomach are often entirely wanting. Failure of the bile or of the pancreatic secretion to enter the bowel occasionally causes diarrhea by favoring putrefactive decomposition of the intestinal contents.

**Diarrhea in General Diseases.**—Various acute infections may be accompanied by diarrhea even though the intestinal tract itself is not directly involved. The excitant in these cases is probably the toxins eliminated by way of the bowel. The diarrhea sometimes observed in nephritis has been ascribed to the irritant action of ammonium carbonate derived from urea vicariously excreted by the bowel. Diarrhea not infrequently complicates leukemia, pernicious anemia and purpura abdominalis (Henoch's purpura).

**Nervous Diarrhea.**—Certain diseases affecting the nervous system, such as hyperthyroidism, hysteria and neurasthenia, are sometimes associated with recurring attacks of diarrhea. The latter apparently does not depend upon any definite anatomic changes in the intestine, but originates in accelerated peristalsis or in excessive transudation of serum. The stools are usually watery and not rarely the defecation occurs immediately after taking food or follows emotional excitement. Occasionally no other nervous

phenomena are present and diarrhea is the only symptom. The disease known as mucous colic is regarded by some authors as an intestinal neurosis with excessive formation of mucus.

**Bacteriology.**—Among the various microörganisms that may be concerned in the production of diarrhea the most important are the Bacillus coli communis, the Bacillus dysenteriæ (Shiga) and allied forms, the Bacillus enteritidis of Gaertner, the paratyphoid bacillus, staphylococci and streptococci. Less frequently the Bacillus pyocyaneus, the Bacillus botulinus, or the Bacillus aërogenes capsulatus is the active agent.

Diarrhea may result also from invasion of the intestines by certain protozoa, such as endamebæ, cercomonads, trichomonads, lamblia, etc.

**Diagnosis.**—The diagnosis of the acute forms of diarrhea is, as a rule, readily made, although it may be difficult to determine without recourse to bacteriologic methods whether an enteritis is one of the ordinary type or dysenteric. In chronic diarrhea an exact diagnosis can only be made by careful investigation of the whole case, including the examination of the feces. Schmidt's method is simple and has much to recommend it. This method requires the use of a test diet which contains known amounts of its various constituents. Knowing what the stools should be with this so-called "normal diet," it is not difficult to detect abnormalities in the digestion of connective tissue, muscle fibre, starches and fats. Even macroscopic examination of the stools sometimes affords valuable information. Thus, mucus in considerable quantities, fresh blood, and pus point to the large intestine as the site of disease. Mucus in small particles, intimately mixed with the feces and stained with bilirubin, is usually from the lower part of the small intestine. Mucus from the upper part of the alimentary tract is digested in the lower portion and so does not appear in the feces.

Carcinoma of the colon as a cause of chronic diarrhea is very likely to be overlooked, as in many instances the symptoms are in no way characteristic. Errors in diagnosis would often be avoided if in every doubtful case pains were taken to make a digital examination of the rectum and to supplement this, if necessary, by proctoscopy.

## ACUTE ENTERITIS

(Acute Ileocolitis; Acute Inflammatory Diarrhea)

**Definition.**—This is an acute inflammation of the intestinal mucous membrane, affecting chiefly, as a rule, the small bowel, but not rarely extending throughout the entire intestinal tract. The terms duodenitis, jejunitis, ileitis, etc. are applied to anatomical subdivisions of the process, but clinically it is not always possible to determine accurately the site of the lesions.

**Etiology.**—Acute enteritis occurs at all ages and in all seasons, but it is most frequent in children and most prevalent during hot weather. In the majority of cases the disease is due to the action of irritants contained in food (unripe fruit, tainted meat, etc.) or formed in the alimentary canal as a result of indigestion. Bacteria play an important rôle in the process, the chief offender being the ordinary colon bacillus, this organism apparently becoming more virulent and aggressive in the presence of digestive disturbances. In some localities contamination of food by flies may be directly responsible for attacks of acute enteritis. Chilling of the body favors the occurrence of the disease. A less frequent cause is the ingestion of irritant

drugs or poisons. As a symptomatic condition enteritis occurs in many acute infections (typhoid fever, cholera, dysentery, tuberculosis, etc.), in certain auto-intoxications (uremia), and in various visceral diseases causing passive congestion of the bowel (chronic heart disease, cirrhosis of the liver, etc.).

**Morbid Anatomy.**—During life the mucous membrane of the intestine is swollen, congested and covered with flakes of mucus, but at necropsy these changes may not be marked. In severe cases the follicles are prominent and sometimes the seat of superficial erosions or of actual ulcerations. Small hemorrhagic extravasations may also occur. Microscopically, there is infiltration of the mucosa and submucosa, with excessive formation of goblet cells, and desquamation of both superficial and glandular epithelium.

In certain intense forms of the disease the inflammation is attended by the formation of a fibrinous or croupous exudate (*pseudomembranous* or *diphtheritic enteritis*), or very rarely by a purulent infiltration, circumscribed or diffuse, of the submucosa (*phlegmonous enteritis*).

**Symptoms.**—In the milder cases diarrhea is the chief symptom, and even this may be slight if the inflammation is confined to the duodenum or jejunum. The stools are more or less liquid, vary in color from dark brown to pale yellow or grayish-white, and range in number from three or four to twenty or more in the day. Other intestinal disturbances, such as colicky pain, abdominal tenderness, borborygmi, and tympanites, frequently precede or accompany the diarrhea, and in the more severe cases, especially if the upper portion of the small bowel is affected, symptoms of gastric irritation may also be present. Some degree of fever, indicated subjectively by a sense of chilliness, increased frequency of the pulse, and general lassitude, is often observed. The urine is reduced in quantity and may contain a small amount of albumin and a few hyaline or granular casts.

A very severe form of the disease, bearing a close resemblance to Asiatic cholera and usually known as *cholera morbus* or *cholera nostras*, is occasionally encountered. This type of enteritis generally occurs in summer and affects chiefly young adults. It develops suddenly and is characterized by violent cramp-like pains in the abdomen and calves of the legs, persistent vomiting, extreme thirst, frequent and copious watery stools, and the early supervention of marked prostration or even of actual collapse.

**Diagnosis.**—The diagnosis is usually made without difficulty, although occasionally typhoid fever or appendicitis may come into question. The distinguishing features of *typhoid fever* are the gradual onset, step-like rise of temperature, bronchial catarrh, splenic enlargement, leucopenia, and after the first week, the rose spots and Widal reaction. *Appendicitis* is not likely to cause confusion unless it is accompanied by diarrhea; even then the increasing tenderness and rigidity in the right iliac region, the repeated vomiting and definite leucocytosis will usually make the diagnosis clear. The differential diagnosis between *bacillary dysentery* and ordinary forms of ileocolitis must rest upon the positive agglutination reaction of the dysentery bacillus with the patient's blood serum or the isolation of the bacillus from the stools. Likewise, bacteriologic methods afford the only means of distinguishing between choleraic types of enteritis and mild attacks of *true cholera*, when the latter is prevalent.

As regards the *site of the inflammation*, marked gastric symptoms, borborygmi, and greenish or yellowish stools intimately mixed with small particles of mucus and containing undigested food indicate involvement of the small bowel; whereas tenderness along the course of the colon, tenesmus, and small frequent stools containing much free mucus point to involvement

of the large bowel. Duodenal catarrh is sometimes suggested by the occurrence of jaundice.

**Prognosis.**—Attacks of acute enteritis last, as a rule, from a few days to two weeks, and usually end in recovery. In debilitated subjects and infants, however, the disease often assumes a grave aspect and may prove fatal. In some instances the condition becomes subacute or chronic.

**Treatment.**—Rest in bed, a light diet (boiled milk, arrowroot, milk toast, etc.), and the administration of an unirritating purgative, such as castor oil, calomel in fractional doses, or Epsom salt (unless the bowels have been already thoroughly emptied) are all that is required in mild cases. In robust subjects it is even better to withhold all food for twenty-four or thirty-six hours. Severe cases require additional measures. Externally, stupes or sinapisms afford much relief. Internally, the most generally useful remedies are mild astringents, such as bismuth subnitrate or chalk, in fairly large doses (20 gr.—1.3 gm.), and opium, in the form of morphin, codein, or paregoric. Combinations of these drugs with so-called intestinal antiseptics (salol, creosote, etc.) are often efficacious:

℞. Codeinæ sulphatis ..... gr. ii (0.13 gm.)
Phenylis salicylatis ..... gr. xxiv (1.5 gm.)
Bismuthi subnitratis ..... ℥ss (15.0 gm.) M.
Fiant chartulæ No. xii.
Sig.—One powder every three hours.

℞. Phenylis salicylatis ..... gr. xxiv (1.5 gm.)
Tincturæ opii camphoratæ ..... f℥ss (15.0 mils)
Misturæ cretæ ..... q. s. ad f℥iii (90.0 mils) M.
Sig.—Dessertspoonful every three hours.

Active astringents, such as the preparations of tannin, lead acetate, and silver nitrate, are usually unnecessary, but occasionally if the evacuations are very frequent and copious they may be given with advantage. A combination such as the following may be prescribed:

℞. Codeinæ sulphatis ..... gr. ii (0.13 gm.)
Tannalbin ..... ℥i (4.0 gm.)
Bismuthi subcarbonatis ..... ℥ss (15.0 gm.) M.
Fiant chartulæ No. xii.
Sig.—One powder every three hours.

In the choleraic forms of diarrhea the cramp-like pains are best controlled by subcutaneous injections of morphin (gr. 1/12–1/4—0.005–0.016 gm.), or in less severe cases by carminatives with opium by the mouth. Such a combination as the following is often useful:

℞. Spiritus camphoræ ..... f℥ij (8.0 mils)
Spiritus chloroformi ..... f℥ss (15.0 mils)
Tincturæ opii camphoratæ ..... f℥vi (22.0 mils)
Aquæ menthæ piperitæ ..... q. s. ad f℥iii (90.0 mils) M.
Sig.—Dessertspoonful every hour or every 2 hours.

When the colon is especially involved local treatment is advisable. Cleansing enemas of normal salt solution may be given several times a day and followed by injections of warm starch water (one to two ounces). Laudanum (20 min.—1.2 mils) is often added to the starch water, although the opium, of course, has no local action. Tenesmus may be relieved by ice suppositories, inserted at short intervals, or by injections containing cocain (10 min—0.6 mil of a 4 per cent. solution).

With the cessation of the diarrhea increase of food may be allowed, but the return to ordinary diet should always be effected slowly.

## CHRONIC ENTERITIS

**Etiology.**—Chronic inflammation of the intestine may result from an attack or a series of attacks of acute enteritis, or it may develop gradually as a consequence of persistent irritation of the bowel. Among the chief causes of the latter may be mentioned: (a) abnormal intestinal contents, arising from errors of diet or faulty digestion; (b) passive hyperemia of the bowel from cirrhosis of the liver, chronic heart disease, etc.; (c) specific bacterial or protozoan infection of the intestine (tuberculosis, bacillary dysentery, amebiasis, trichomoniasis, etc.; (d) metazoan infection of the intestine—worms; (e) chronic constipation and mechanical irritation by scybala; (f) other organic diseases of the bowel (carcinoma, stricture, etc.; (g) various chronic diseases not directly involving the intestine, such as pulmonary tuberculosis, diabetes, chronic nephritis, malaria, etc. (indigestion, passive hyperemia, or excretion of irritants into the bowel).

**Morbid Anatomy.**—The lesions vary considerably according to the form and duration of the disease.

Generally speaking, however, the process is either hypertrophic or atrophic. In many cases the mucous membrane is thickened and congested, and of a dark gray color from hemorrhagic pigmentation. Hemorrhages and erosions are often seen. The glandular tubules may be enlarged and distended with mucus, the accumulation of secretion sometimes leading to the formation of small cysts. Occasionally, wart-like or polypoid excrescences make their appearance, either singly or in groups. In other cases, owing to the predominance of atrophic changes, the intestinal wall throughout is distinctly thinner than normal and the mucosa is smooth and pale, and darkened here and there with blood-pigment. Histologically, the lesions in all cases are those of interstitial inflammation with parenchymatous degeneration.

**Symptoms.**—The only constant symptom is irregular action of the bowels, the type of irregularity depending upon the intensity and localization of the inflammatory process. In one group of cases there is pronounced constipation; in another group there is constipation alternating at intervals of several days or weeks with diarrhea, and in a third group there is persistent diarrhea. Catarrh of the entire intestinal tract is almost always associated with diarrhea. Whatever the consistence or frequency of the evacuations, mucus in large or small amounts is always present unless the inflammation is strictly confined to the small intestine, which is exceptional. Less constant symptoms of the disease are colicky pains, borborygmi, flatulence, abdominal tenderness, and, in the event of the rectum being involved, tenesmus.

Various nervous phenomena, such as apathy, lassitude, psychic depression, irritability, and palpitation of the heart are often present. The general health is usually more or less impaired, but it may be well maintained if the large bowel only is affected. As regards the localization of the catarrh, anorexia, nausea, marked borborygmi and meteorism, and stools free from mucus but containing bilirubin (green reaction with sublimate test) and many undigested muscle fibers and starch cells indicate involvement of the small intestine. An intimate admixture of small particles of mucus with solid, semi-solid or liquid stools points to an affection of the lower part of the ileum and upper part of the colon. Tenderness along the course of the colon and stools of firm consistency coated with a layer of mucus suggest colitis, while the occurrence of tenesmus and the passage of pure mucus indicate proctitis, or inflammation of the rectum. Diarrhea rarely occurs in chronic colitis unless an ulcerative process is present. Macroscopic pus comes from the large bowel and points to ulceration. Putrefying, dark colored, fluid stools, if

persistently present, are suggestive of a gross lesion, such as dysenteric or malignant ulceration.

**Diagnosis.**—No sharp line of distinction can be drawn between chronic enteritis on the one hand and *dyspeptic diarrhea* and *mucous colic* on the other; indeed, dyspeptic diarrhea is often followed by a true catarrh and many authorities (Boas, von Noorden, Tuttle) maintain that mucous colic is always associated with definite lesions in the bowel. The exclusion of a specific form of enteritis in tuberculous and syphilitic cases with persistent diarrhea may be a difficult matter, the course of the intestinal disturbance or the effect of treatment often affording the only means of reaching a definite conclusion. *Amebic dysentery* is distinguished with certainty from the ordinary type of chronic enteritis by the detection of the entamebæ in the stools. Chronic diarrhea may be for a long time the only prominent symptom in *carcinoma of the rectum*, for this reason a careful digital examination, supplemented, if necessary, by proctoscopy, should be made in every doubtful case.

**Prognosis.**—Marked improvement often follows continuous treatment, and complete recovery, although exceptional, is possible if the noxious agency that primarily caused the enteritis ceases to act before serious structural changes have been produced in the wall of the bowel. The disease usually lasts for years and, except in debilitated subjects and young children, is rarely the direct cause of death.

**Treatment.**—The cause must be ascertained and removed, if possible. The diet, clothing, habits, occupation, and mode of living of the patient should receive careful attention. The diet is especially important, and the best basis for the appropriate regulation of it, at least as regards particular articles of food, is afforded by systematic examination of the stools after the use of a Schmidt test diet. In all cases the food should be bland, well cooked, and finely divided. Foods that are coarse and leave much residue are inadmissible. Patients with persistent diarrhea sometimes do well on an exclusive milk diet. When the disease is not very severe and is confined for the most part to the colon, a selected mixed diet may be allowed. The patient's body should be well protected against chilling, and as an additional safeguard a woolen abdominal bandage may be worn with advantage. In severe cases with persistent diarrhea rest in bed for a time may be essential. In milder cases with slight diarrhea or a sluggish condition of the bowels much benefit may be derived from a change of scene and air and carefully graded exercise. To these factors, as well as the strict dietetic regimen to which the patient is subjected, is to be ascribed much of the good that is often obtained from a sojourn at certain health resorts, such as Carlsbad and Vichy in Europe and Hot Springs, Va. and Bedford Springs, Pa., in this country.

As regards medicinal treatment, mild astringents are usually indicated if there is much diarrhea. The most suitable of such remedies are bismuth subnitrate and prepared chalk. If there is marked fermentation small doses of one of the so-called intestinal antiseptics (salol or betanaphthol) may be used as an adjuvant. If the stools are very frequent and watery some preparation of tannin, preferably tannigen or tannalbin, may also be given with advantage. A combination such as the following is sometimes efficacious.

℞. Bismuthi subnitratis ..... ℥v (20.0 gm.)
Phenylis salicylatis..... ℥ss (2.0 gm.)
Tannalbin..... ℥j–℥jss (4.0–6.0 gm.) M.
Fiant Chartulæ No. XX.
Sig.—One powder after meals.

If there is much pain a small amount of codein may be added to this formula. Warm fomentations are useful during acute exacerbations. In

the milder cases silver nitrate, combined with extract of opium and administered in keratin-coated pills, is sometimes very efficacious. In case of deficient or absent gastric secretion hydrochloric acid should be given in large doses. In enteritis associated with constipation, saline laxatives are of value. From ½ to 1 teaspoonful of Carlsbad salts may be dissolved in a tumblerful of hot water and taken on an empty stomach early in the morning. Drastic cathartics should be avoided. When the colon is chiefly involved, irrigation of the bowel is very useful. Sterile water, normal salt solution, or a solution of silver nitrate (1 to 5000) may be used for the purpose.

## DIARRHEAL DISORDERS OF EARLY CHILDHOOD

Diarrhea is especially common in early childhood, about one-fourth of the total deaths occurring in the first year of life being due to this cause. After the second year the incidence is greatly reduced. The largest number of cases occur during the summer months. Overcrowding, uncleanliness, and poverty are important predisposing factors. Artificially fed infants and the constitutionally weak are particularly susceptible. Food that is unsuited to the child, such as an excess of carbohydrate, of fat, or of protein, or food that is qualitatively changed as a result of bacterial action is alone capable of producing the disease. Now that milk is more carefully handled and is usually pasteurized, severe gastro-intestinal disturbances in children have become less common. Many cases of diarrhea, particularly of the inflammatory form, are caused directly by well recognized bacteria, for example, the Bacillus dysenteriæ, the gas bacillus, the colon bacillus, Bacillus pyocyaneus, and streptococci.

**Varieties.**—For clinical purposes the following types of diarrhea in infants may be recognized: (1) Dyspeptic diarrhea; (2) cholera infantum (acute gastro-enteric intoxication); (3) acute ileocolitis. It must be borne in mind that these types shade into one another, and that in many cases dyspeptic diarrhea, either through neglect or a lack of resistance in the patient, develops into ileocolitis or, more rarely, into cholera infantum.

**Morbid Anatomy.**—The changes vary considerably both in kind and in degree. In many of the milder cases there are no important lesions. In other instances the intestinal mucosa is congested or abnormally pale, and microscopic examination reveals more or less pronounced degenerative changes in the epithelium. Not rarely the liver and kidneys share in the degenerative process. In well-marked ileocolitis the mucosa, especially that of the lower part of the ileum and that of the colon, is congested, swollen, and dotted here and there with areas of epithelial exfoliation and petechial hemorrhages. The solitary and agminated lymphoid follicles are usually enlarged and in severe cases there may be many sharply defined ulcers, some originating in solitary follicles and others in the mucosa itself. The mesenteric lymph nodes are also swollen and as a rule the parenchymatous organs show degenerative changes.

The pronounced systemic intoxication that frequently attends severe gastro-intestinal disorders in children may be due to the absorption of bacterial toxins or products resulting from the decomposition of food or to acidosis.

**Symptoms.** *Dyspeptic Diarrhea.*—In this form the stools vary in number from 2 or 3 to 12 or more in the twenty-four hours. They are offensive, of a pale yellow or greenish color, and usually contain undigested curds of milk,

but no blood and little or no visible mucus. Vomiting occurs in most cases, but it is not often persistent. The temperature ordinarily ranges between 100° and 103° F. Not rarely, however, it is much higher at the onset. Prostration is not very pronounced and nervous symptoms usually consist merely of irritability and restlessness.

*Cholera Infantum.*—This is the rarest but the gravest form of summer diarrhea. It may appear suddenly or develop abruptly in the course of an ordinary dyspeptic diarrhea. In the first instance vomiting and purging begin almost simultaneously and become incessant. The stools are watery and copious. Thirst is intense. The temperature in the rectum is high, often 105° or 106° F., although it may be low at the surface of the body. The urine is scanty and albuminous or suppressed. Collapse soon follows, and is shown by pinched features, hollow eyes, sunken fontanel, pallid skin, and cold surface. Even at this time a reaction may set in, but in the large majority of cases death results in from 24 to 72 hours. Toward the close of life stupor, convulsions and coma (meningismus) not rarely supervene. With the occurrence of a reaction the picture may gradually merge into that of acute ileocolitis.

*Acute Ileocolitis.*—This may begin as a primary condition or succeed an ordinary dyspeptic diarrhea. The stools are numerous but usually small, and consist chiefly of green mucus, streaked with blood. Occasionally there is considerable bleeding. The abdomen is distended and tender. The temperature, as a rule, ranges between 103° and 104° F., but it may be lower. Vomiting is common, although it is usually a less obtrusive feature than in the dyspeptic or the choleraic form. Colicky pains frequently precede the stools and almost always there is pronounced tenesmus. Prolapse of the rectum may occur. Bacillus dysenteriæ is found in some of the cases, but other organisms are capable of producing the disease. Weakness and emaciation more or less rapidly ensue and in unfavorable cases the child eventually sinks into a state of collapse or passes into a marantic condition persisting several days. Death is frequently preceded by delirium, stupor and coma. The disease may terminate favorably or unfavorably within a week or ten days, but in the majority of cases it lasts from 2 to 6 weeks. It is always serious, especially in infants below the normal physical standard, and even in favorable cases convalescence is likely to be slow. Relapses, too, are common.

**Complications.**—Bronchopneumonia and suppurative otitis are not uncommon in the more severe and protracted cases. Various forms of stomatitis may develop. Albuminuria and cylindruria are frequently observed in acute ileocolitis, but actual nephritis is unusual. Acute infectious diarrhea is not rarely followed by chronic ileocolitis.

**Diagnosis.**—It is often difficult and sometimes impossible to distinguish between *dyspetic diarrhea*, if severe, and *acute ileocolitis*. However, persistent fever, the occurrence of tenesmus, and the presence of blood and of much mucus in the stools always point strongly to the latter.

*Intussusception* is also attended by mucous and bloody stools, but in this disease the onset is abrupt, fever is absent at the beginning, fecal matter disappears entirely from the evacuations, and in the majority of cases a tumor is recognizable by abdominal or by rectal palpation. Meningismus occurring in summer diarrhea may closely simulate *meningitis*. In the latter, however, diarrhea is exceptional and the spinal fluid is characteristically changed.

**Treatment.**—Much can be done to prevent the occurrence of diarrhea in infants during the summer season. The most important elements in prophy-

laxis are: the avoidance of weaning in the late spring or summer; the use of suitably modified milk in artifically fed infants; the pasteurization of all milk and reduction of the strength of the mixture during very hot weather; regularity in the hours of feeding; absolute cleanliness of the feeding apparatus and of the mother's or nurse's hands before touching the food; the supply of an abundance of fresh air; daily bathing and on hot days frequent spongings; the avoidance of chilling; and the immediate correction of slight digestive disorders.

At the first sign of intestinal disturbance milk should be withdrawn at once whether the infant is breast-fed or bottle-fed and not resumed for at least 24 hours. It is necessary, however, to give water freely, either as such or in the form of barley-water, rice-water, or strained broth. The return to milk must be made with caution. To remove irritant matter from the bowel, castor oil (2 drams—8.0 mils) or calomel should be given. Irrigation of the colon with normal saline solution once or twice in the twenty-four hours is also useful, especially in ileo-colitis. If the bowel is very irritable the water may be introduced at a temperature of 105° F. In other cases better results are usually secured with cool water (80°–90° F.). With persistent fever and frequent stools it may be necessary to repeat the laxative. In most cases it is necessary to follow the laxative with a mild astringent, such as bismuth subcarbonate or chalk. The former is usually preferable and may be given in doses of 10 grains (0.65 gm.), suspended in cinnamon water or peppermint water, at two-hour intervals. A more active astringent, such as tannalbin (1–2 grains—0.065–0.13 gm.), may be given in addition to the bismuth or chalk if the discharges are very profuse and watery, although it is rarely required.

Opium is often of value, but great caution must be exercised in its use. It is indicated when the diarrhea persists despite the thorough unloading of the bowel and the use of mild astringents, and when pain or tenesmus is pronounced. Paregoric in doses of 5 to 10 minims (0.3 0.6 mil.), every 2 to 4 hours, is, as a rule, the best preparation. It may be added to the bismuth, but owing to the necessity of a frequent change of dosage, it is better not combined with the astringent in the same prescription. If the stomach is unretentive tincture of opium (2–3 minims—0.12–0.2 mil) may be given by enema. The starch enema (1–2 ounces—30.0–60.0 mils) is a time-honored remedy for severe tenesmus. It is made by mixing into a smooth paste a dram (4.0 gm.) of starch with a little cold water and then adding boiling water until a mucilage is formed. Laudanum is often added to starch mucilage, but its action is, of course, purely central. The application of hot stupes or compresses to the abdomen frequently renders the use of opium unnecessary. In persistent colitis injections of silver nitrate (1:1000) are sometimes useful.

Stimulants are not rarely required. The best are tincture of nux vomica in doses of 1 minim (0.06 mil), equal to $\frac{1}{400}$ grain (0.00016 gm.) of strychnin, for an infant of 1 year; caffein-sodium benzoate, $\frac{1}{4}$–$\frac{1}{2}$ grain (0.016–0.03 gm.), by mouth or subcutaneously; camphor, $\frac{1}{2}$ grain (0.03 gm.) in oil, subcutaneously; and brandy or whisky, 5–15 minims (0.3–1.0 mil) well diluted with sweetened water, by the mouth.

Temporary removal to the seashore or mountains is often of the greatest benefit when the disease loses its acute character but tends to persist.

In *cholera infantum* the stomach should be washed out with cool water and the bowel irrigated. As a rule, however, neither process should be repeated. At first nothing should be given by the mouth but cold water and brandy or whiskey. If the stomach is wholly unretentive stimulants should

be given hypodermically. If the temperature is low hot baths (105° F.), lasting 5 minutes, may be given at frequent intervals. On the other hand if the temperature is high cool packs (85° F.) should be substituted. Colonic irrigation with cool water (90°–80° F.) also aids in reducing pyrexia.

Persistent vomiting and purging are best treated by morphin and atropin hypodermically. For a child of 1 year 1/100 grain (0.00065 gm.) of morphin may be given with 1/600 grain (0.0001 gm.) of atropin, and repeated as required, but not more frequently than once in 3 hours. In desperate cases normal salt solution should be used subcutaneously, from 2 to 3 ounces (60.0–90.0 mils) being injected 3 or 4 times a day.

After vomiting has ceased, barley-water, albumin-water, or fresh beef-juice may be given by the mouth. Milk feeding should always be resumed very cautiously.

## CHRONIC ULCERATIVE COLITIS

Chronic ulcers in the colon may usually be classed as follows: (1) Tuberculous, (2) dysenteric, (3) syphilitic, (4) carcinomatous, (5) stercoral (6) uremic and (7) simple. Ulceration of the colon occasionally occurs also in mucous colitis, pellagra, leprosy, actinomycosis, and leukemia.

The term **simple ulcerative colitis** is used to designate those cases, not very uncommon, in which the lower bowel is the seat of ulcers that cannot be associated with any definite cause. Some observers have assumed that such ulcers are the remains of an extinct amebic or Flexner-Shiga bacillary infection, but their etiology is not really known. The rectum is usually the part of the bowel most extensively ulcerated, but in the majority of cases the sigmoid and descending colon are also involved. Occasionally, lesions are found throughout the colon and even in the lower part of the ileum.

The disease is most common in adolescence and early adult life. Of 117 cases analyzed by Logan[1] of the Mayo Clinic, 74 were in males and 43 in females.

**Symptoms.**—The disease may begin suddenly or gradually and either as an ordinary diarrhea or as a colitis. The stools at first are watery, but later contain mucus, blood and pus. The number of evacuations varies from 3 or 4 to 12 or more in the twenty-four hours. Tenesmus is frequently present, and in many cases there is complaint of abdominal pain or soreness and of flatulence. Fever is rarely observed. The general health may be well maintained for several years, but sooner or later anemia, weakness, and emaciation supervene. The symptoms may be continuously present or remittent. Proctoscopic examination often reveals the lesions when the process affects the rectum and sigmoid and the x-ray when it affects the colon itself. The diagnosis of the disease is based on the existence of chronic ulceration of the colon with negative bacteriologic findings.

**Prognosis.**—The outlook is serious, although the duration of the disease is usually long (several months to many years), and a cure is by no means impossible. Even when healing of the ulcers occurs, however, the contraction of the scars may result in partial obstruction of the bowel. In unfavorable cases death may be due to suppurative peritonitis, localized or diffuse, or intercurrent disease, especially pneumonia.

[1] Collected Papers of the Mayo Clinic, 1918, x.

**Treatment.**—The treatment is mainly that of the specific forms of ulcerative colitis. The diet should consist of foods that are unirritating and leave little residue in the colon. Rest and adequate protection of the abdomen are important measures. Internal medication is not very effective. Large doses of bismuth subnitrate (30 grains—2.0gm.), three or four times a day, however, sometimes afford temporary relief. At the Mayo clinic the greatest benefit was obtained from enemas of hot water (120° F.). These were given twice daily for 20 to 30 minutes, a double rectal tube being used so as not to distend the bowel.

Silver nitrate enemas (1 : 10,000 gradually increased to 1 : 1000) have also been found more or less useful. As a means of securing thorough irrigation of the colon and of preventing irritating material from passing over the ulcerated surface, appendicostomy and especially cecostomy or ileostomy have been performed with some success.

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## MUCOUS COLITIS

**(Myxomembranous Colitis; Mucous Colic)**

Mucous colitis is a chronic condition occurring chiefly in neurotic subjects, characterized by the excessive formation of mucus in the colon, and usually manifested by paroxysms of abdominal pain, which disappear at once upon the discharge of the mucus.

The disease is much more common in women than in men, and occurs most frequently in middle life, although it has been observed both in childhood and in old age. Neurotic, neurasthenic or hypochondriacal persons are the chief sufferers. Constipation or intestinal stasis seems to be a contributing factor in many instances. Mucous colitis may occur as an independent condition, but in many cases, probably the majority, it is intimately associated with some other intra-abdominal lesion, such as visceroptosis, chronic appendicitis, peritoneal adhesions, carcinoma of the bowel, and in women, various disorders of the generative organs. The frequent association of visceroptosis with mucous colitis has been mentioned by a number of writers (Ewald, Glènard, de Langenhagen, Einhorn, Kemp). Twenty-one of Hale White's[1] 51 female patients had some disorder of the pelvic organs and 5 had membranous dysmenorrhea. The nature of the process is obscure. Some investigators believe the disease to be of catarrhal origin; others class it as a secretory neurosis (*myxoneurosis*); while a third group conclude that there are two entirely different conditions, one an inflammatory disease with the production of an excessive amount of mucus, the other a purely nervous disturbance without structural change in the bowel. Autopsies in the cases of O. Rothmann and Osler (Edwards) gave negative results, but those in the cases of M. Rothmann and Hemmeter disclosed signs of catarrhal inflammation.

**Symptoms.**—The most characteristic symptom of the disease is the passage from the bowel of large quantities of mucus. This occurs usually in paroxysms, which, as a rule, are preceded or accompanied by severe abdominal pain of a cramp-like character. Generally there is more or less abdominal tenderness with the pain, and not infrequently contracted segments of the colon may be palpated. In some instances pain is entirely absent. The mucus occurs as jelly-like masses, fibrinous shreds, membranous casts of the bowel, or tape-like strips, suggesting portions of a tapeworm. The color of

[1] Lancet, Oct. 28, 1905.

the mucoid material is generally gray, but it may be brown from admixture with feces or rarely red from admixture with blood. Histologically, the membranes consist of a homogeneous ground-substance interspersed with various intestinal débris—degenerated epithelial cells, particles of undigested food, leucocytes, bacteria, cholesterin crystals, etc. In some instances the stools also contain intestinal sand. This was noted in 112 of 1200 cases of mucous colitis analyzed by de Langenhagen.[1] The attacks may occur daily for several days, a week or even a longer period, and the free intervals may last a few weeks or several months. Many patients associate their attacks with emotional disturbances, fatigue, dietetic errors or chilling of the body.

Constipation is the rule in the free intervals, but occasionally diarrhea and constipation alternate. Even when the bowels seem freely open colonic irrigation may reveal the presence of much putrefactive material. Digestive disturbances of various types are usually present, and most of the subjects are nervous, intraspective, self-conscious, neurasthenic or hypochondriacal. Not a few are bedridden invalids. Bronchial asthma, urticaria and angioneurotic edema are occasionally observed as complications. The disease is very resistant to treatment and may persist for many years. It sometimes leads to pronounced weakness and emaciation, but it rarely of itself proves fatal. However, a few instances of fatal syncope have been reported (Herringham, Journeault). Permanent recovery occurred in about 50 per cent. of the cases analyzed by von Noorden and by Hale White.

The **diagnosis** of mucous colitis rests on the occurrence of mucous masses, shreds or casts in the stools, usually in association with paroxysms of abdominal pain, but unaccompanied by other indications of intestinal inflammation. If the mucus is retained in the bowel it may usually be made to appear in the stools by the administration of a full dose of castor oil. In some cases the colicky pain is so severe and so definitely localized that appendicitis, intestinal obstruction, renal calculus, cholelithiasis, floating kidney (Dietl's crises), or plumbism is suggested. Occasionally a microscopic examination may be required to differentiate undigested pieces of meat, membranes of fruit, etc. from mucous shreds. After the diagnosis of mucous colitis has been made it is important to determine whether the disease is primary or is secondary to some other condition, such as chronic appendicitis, carcinoma, etc.

**Treatment.**—Dietetic measures play an important part in the treatment, but no one kind of diet is suitable for all cases and changes must frequently be made to meet special indications. Generally speaking, the diet should be liberal, solid rather than liquid, and unirritating. The diet of coarse foods, recommended by von Noorden, has not had many advocates in this country, but it may prove serviceable if the attending constipation is atonic rather than spastic. All writers are agreed that the establishment of a normal action of the bowels is absolutely essential to the achievement of a permanent cure. For this purpose, in addition to dietetic regulations, it is usually necessary to employ laxatives or intestinal irrigation, as well as the physical measures described under Habitual Constipation, and to continue them for several months after apparent recovery. Castor oil, if well received by the stomach, is one of the best laxatives. It should be given in doses of from ½ to 1 ounce (15.0–30.0 mils) in the early morning. In some cases liquid petrolatum may be substituted for the castor oil with advantage. In other cases cascara sagrada or a combination of this remedy with agar acts satisfactorily. Salines are less efficacious, as a rule, and drastic purgatives are contraindicated. Colon-irrigation, several times a week with normal

[1] M. de Langenhagen, Mucomembranous Enterocolitis, 1903.

saline solution (100° F.) or a solution of sodium bicarbonate (a teaspoonful to a liter of water), if practised regularly, often affords much relief. For many years at Plombières and Chatel-Guyon in France and at Harrowgate in England treatment by intestinal irrigation has been carried out with excellent results. Occasionally, lavage of the colon seems to increase the secretion of mucus. In such cases enemas of bland oil often prove effective and may be given as follows: 200 to 500 mils of slightly warmed linseed, sesame, or olive oil or liquid petrolatum are injected at first every night, then, after three weeks, every other night, and later with decreasing frequency. The injections should be given slowly through a soft rubber tube, the patient remaining on the left side for ten minutes. If possible, the oil should be retained overnight.

Measures to improve the patient's general health are almost always required. A modified or partial Weir Mitchell rest cure is of much benefit in some cases; in others systematic exercise in the open air, provided it is not too fatiguing, yields better results. A change of scene is often helpful. Hydrotherapy is of considerable value. Tonics, such as iron, arsenic, and nux vomica, are useful as occasion may demand. In some instances the bromids for a short time, either alone or in association with belladonna, seem to be of service. Any associated abdominal condition, such as appendicitis, adhesions, cholecystitis, etc., should receive appropriate treatment, but radical measures should be avoided unless the indications are very definite. If visceroptosis is a prominent feature a straight-front supporting corset or Rose's adhesive plaster belt may accomplish much good. Finally, in very severe and otherwise intractable cases surgical measures that will facilitate irrigation of the entire colon, such as cecostomy, or tend to remove intestinal stasis, such as partial colectomy, may have to be considered.

In *the attacks of severe colic*, rest in bed, the application of heat to the abdomen, the administration of a full dose of castor oil and of belladonna, with codein, if necessary, colonic irrigation with a solution of sodium bicarbonate or the use of a warm oil enema are the measures that afford the most relief.

## APPENDICITIS

**Etiology.**—Inflammation of the vermiform appendix is one of the most common of the intra-abdominal diseases. To account for this it is only necessary to consider the rudimentary character of the organ, its situation with relation to the cecum, its small lumen, poorly developed muscular coat, and rich supply of lymphoid tissue.

Acute appendicitis occurs at all ages, but young persons are especially susceptible, the large majority of cases occurring between the ages of 10 and 35. In 1917 Abt[1] collected 80 cases in children under 2 years of age. The disease is rare after 60. Males are affected somewhat more frequently than females. It is probable that chronic indigestion and habitual constipation predispose to the disease. The determinative cause of acute appendicitis is not always apparent; sometimes it is chilling of the body, and occasionally it is trauma. Recent observations (Poynton and Paine, Kretz, Rosenow) seem to indicate that exceptionally the disease is of hematogenous origin and secondary to some distant focus of infection, in which the inciting organisms have acquired an elective affinity for the appendix. This view offers an

[1] Arch. of Ped., 1917, xxxiv, 641.

explanation of the occasional occurrence of appendicitis after tonsillitis and other throat infections. Appendicitis may occur as a complication or sequel of typhoid fever. Tuberculous cases are sometimes observed, the lesions in the appendix usually, but not invariably, being consecutive to disease of the cecum. The association of appendicitis and pyosalpinx is not uncommon. In such cases either the appendix or the Fallopian tube may be the primary source of the inflammation.

Fecal concretions are often present in the appendix as the result of a pre-existing catarrh. They do not usually cause acute appendicitis but undoubtedly they may do so by abrading the appendical mucosa and thus favoring the invasion of pathogenic bacteria. Foreign bodies, such as seeds, spicules of bone, pins and lead shot, sometimes lodge in the appendix and set up inflammation, but they are of much less etiological significance than was formerly supposed. The presence of parasitic worms in the appendix, especially Oxyuris vermicularis and Ascaris lumbricoides, must also be regarded as a possible cause of the affection. Pregnancy, while not often responsible for primary attacks of appendicitis, increases the liability to recurrence and renders the disease more dangerous.

Cultures from the tissues of the inflamed appendix usually reveal a mixed infection, the most important organisms being the Bacillus coli communis, Streptococcus pyogenes, and the anaërobic forms. Staphylococci, Bacillus pyocyaneus, Bacillus typhosus, Bacillus tuberculosis, Actinomyces bovis and Entameba histolytica have also been found.

**Morbid Anatomy.**—Acute appendicitis is always one and the same disease, the so-called forms merely representing various stages in development or complications, and unfortunately it is often impossible during the course of the affection to determine the stage that has been reached by the character or severity of the symptoms. In the large majority of cases, and probably in all, the lesions even on the first day of the attack are diffuse, involving all coats of the organ. The inflammatory process may not advance beyond the stage marked by congestion, edema, and slight leucocytic infiltration, but in a large proportion of cases suppuration ensues, with more or less extensive ulceration of the mucosa, and in this event perforation is very likely to occur. In some cases, however, the granulating surfaces unite and eventually through the process of cicatrization the whole appendix is converted into a solid fibrous cord. Obstructions, due to concretions, strictures, kinks, adhesions, etc., favor the accumulation of bacteria and inflammatory matter within the lumen of the appendix and increase the virulence of the infection. In some instances owing to thrombotic occlusion of the blood-vessels or other interference with the blood-supply gangrene supervenes. So rapid may be the course of the disease that within 24 to 48 hours the whole appendix may be transformed into a blackish sloughy mass. In cases associated with concretions there is often localized necrosis or gangrene at the point of pressure.

Appendicitis is clinically important chiefly on account of the peritoneal changes that accompany it. These changes may be limited to the region of the appendix and take the form of fibrinous exudation or of localized abscess (peri-appendicular abscess). The latter is usually the result of perforation, but it may be due to the passage of the bacteria through the walls of the appendix. In other cases owing to perforation of the organ before the formation of adhesions, to rupture of a primary abscess, or, rarely to rapid spread of the infection by extension, there is wide-spread peritonitis with no tendency to limitation.

The situation of abscesses resulting from appendicitis varies according

to the position and length of the appendix. It is usually close to the cecum, but it may be in the pelvis, behind the peritoneum, around the kidney, beneath the liver, or in the subphrenic space. Occasionally it is found in a hernial sac. The pus is usually fetid and may contain fecal concretions or even the sloughing appendix itself. Spontaneous rupture of the abscess may occur into the intestine, especially into the cecum, into the general peritoneal cavity, or through the abdominal wall. Less frequently the pus escapes into some portion of the urinary or genital tract or into the pleural cavity or lung. Even while the abscesses remains intact it may occasion thrombosis of the portal vein and secondary abscesses in the liver or set up general septicopyemia. In a few instances fatal hemorrhage has resulted from ulceration of the internal iliac artery.

**Symptoms.**—Acute appendicitis is usually sudden in onset and characterized in the great majority of cases by the following group of symptoms: Severe abdominal pain, nausea or actual vomiting, tenderness and muscular rigidity on the right side, especially in the region of the appendix, fever (100°–103° F.), acceleration of the pulse, and polymorphonuclear leucocytosis (15,000–25,000). The pain, tenderness and muscular rigidity are in the region of the peripheral distribution of the nerves which in the spinal cord have an intimate relationship with the sympathetic nerves from the appendix—eleventh and twelfth dorsal and first and second lumbar nerves. The pain is usually colicky in character until after the first 36 hours when it becomes a persistent ache. At first it is often diffuse or referred to the central portion of the abdomen, but later it is, as a rule, localized in the right iliac region. In some instances the pain radiates to the right thigh or testicle, and occasionally it is referred chiefly to the lumbar region or to the left iliac fossa. The sudden cessation of pain is not rarely an indication of perforation or gangrene. The tenderness is commonly found in the lower right abdominal quadrant, especially about McBurney's point, which is a point midway on a line drawn from the umbilicus to the anterior superior spine of the ileum and which, according to Mackenzie,[1] is directly over small filaments of the last two dorsal nerves where they pierce the rectus muscle. In some cases, however, owing to the unusual position of the appendix, tenderness may be found only in the lumbar region, in the left iliac fossa, or upon rectal or vaginal examination. When the hyperalgesia is pronounced the patient usually lies quietly on the back or side, with the right thigh flexed. The muscular rigidity in the early stage is generally limited to the lower right abdominal quadrant, but it may be more diffuse even in the absence of spreading peritonitis. The vomiting is a reflex phenomenon and does not often continue for more than 24 hours unless there is extensive peritoneal infection. It affords no relief to the abdominal pain.

Obstinate constipation is the rule, and in nearly all cases there is more or less abdominal distention. Fever is an uncertain indication. While it is present in the great majority of cases, it is sometimes absent from the beginning to the end of the process. A secondary elevation of temperature is strongly suggestive of peritonitis or other complication. As in other acute infections leucocytosis may fail in both very mild and very severe cases. Counts above 25,000 generally indicate a large collection of pus or a complication, such as pylephlebitis. Increased frequency of micturition, retention of urine, or other vesical disturbance is not uncommon when the appendix extends to the pelvis.

In cases which show no definite improvement in 24 or 48 hours the clinical picture usually changes to that of circumscribed abscess or diffuse

[1] Brit. Med. Jour., July 11, 1903.

peritonitis. Peri-appendicular abscess is, as a rule, readily recognized by the appearance of a diffuse or well-defined mass in the right iliac region, with local tenderness and not rarely subcutaneous edema. Unless the abscess is very large fluctuation is not evident. The mass is usually, but not invariably, dull on percussion, and on auscultation yields no peristaltic sounds. Occasionally, owing to the low position of the appendix, no mass is palpable through the abdominal wall, but instead there is a painful swelling within the rectum or vagina. The various systemic disturbances characteristic of local suppuration accompany the abscess, unless the pus is thoroughly encapsulated. The occurrence of diffuse peritonitis is indicated by generalized abdominal pain, tenderness and rigidity, cessation of peristalsis, increasing pulse-rate, persistent vomiting, prostration, and other evidences of septic intoxication. The temperature is variable; in cases of severe infection there is often no fever, but instead profound collapse. Rupture of the appendix, which is usually responsible for the diffuse peritonitis, may be announced by a sudden increase of the abdominal pain, although in many cases it is marked by temporary cessation of pain.

**Diagnosis.**—The diagnosis of acute appendicitis is, on the whole, comparatively easy, but it may be difficult or even impossible if the appendix is in an unusual location. Not rarely one has to take into consideration the possibility of other abdominal conditions causing sudden pain and nausea or vomiting, such as the various colics, acute intestinal obstruction and perforated peptic ulcer. In *renal colic* fever and leucocytosis are usually absent, disturbances of micturition and hematuria are much more common, the pain is more likely to radiate downward and inward toward the groin and into the scrotum, and to be accompanied by retraction of the testicle. In *biliary colic* the location of the pain and tenderness and in many cases the occurrence of jaundice will indicate the true condition. The pain of *simple intestinal colic* does not become localized in the right iliac region, is not accompanied by fever or by tenderness at McBurney's point, rarely leads to vomiting, and is usually of short duration. In *lead colic* the history of exposure to the poison and the presence of other symptoms of plumbism are additionally significant. The occurrence of *acute intestinal obstruction* is usually made evident by diffuse abdominal pain, incessant vomiting, absolute constipation, and absence of febrile symptoms; nevertheless if the condition is rapidly followed by peritonitis it may closely imitate appendicitis. *Perforation* of a *peptic ulcer* may, as a rule, be distinguished by the history, the extremely sudden onset of the symptoms, and the situation of the pain, tenderness and muscular rigidity. In women two important conditions to be borne in mind are ruptured extra-uterine pregnancy and pyosalpinx. The history of suppression or of irregularity of the menstrual periods immediately preceding the attack, the presence of a mass behind and to one side of the uterus, the sighing respiration, extreme pallor and other evidences of internal hemorrhage, and the absence of fever should suggest the possibility of *ruptured ectopic gestation*. The history of previous pelvic disorder, the comparatively slight gastro-intestinal disturbance, and the results of vaginal examination will generally suffice to establish the diagnosis of *salpingitis*, although it must be borne in mind that appendicitis and disease of the uterine adnexa frequently co-exist.

*Lobar pneumonia* at the onset may be readily confused with appendicitis, if the pain is referred to the abdomen, which is not rarely the case in children. Usually in pneumonia, however, the temperature is higher than in appendicitis, the abdominal tenderness more superficial, the respiration more frequent than is consistent with the pulse-rate, the characteristic grunt is present and

physical examination of the chest reveals a pleuritic friction sound or signs of pulmonary infiltration. *Typhoid fever* in the early stages occasionally offers some difficulty, and, as already pointed out, the two diseases may co-exist. *Henoch's purpura*, with abdominal symptoms, may so exactly simulate acute appendicitis that differential diagnosis cannot be made until cutaneous hemorrhages or urticarial wheals make their appearance.

**Course and Prognosis.**—In the majority of cases attacks of acute appendicitis subside. In many cases, too, the patient remains perfectly well afterward. As a rule, however, the appendix is not restored to a normal condition after one attack, and consequently there is very marked tendency to *recurrence*. In the interval between the attacks local symptoms may or may not be present. With the formation of an *abscess* the outlook becomes less favorable, although spontaneous cure may ultimately occur through inspissation of the pus or rupture of the abscess through the abdominal wall or into some passage communicating with the exterior, such as the bowel or vagina. In some instances even though no abscess is found outside of the appendix, the symptoms continue and the disease becomes subacute, owing to the accumulation of pus within the organ, the walls of which have resisted rupture (*empyema of the appendix*). Diffuse suppurative peritonitis, due to rupture of a localized abscess or of the appendix itself, is an exceedingly grave condition under any method of treatment. Apart from the liability to *diffuse peritonitis* the occurrence of suppuration also brings with it the danger of infection in other organs. *Pleurisy* is not uncommon, infection taking place through the lymph-channels or by perforation of the diaphragm. The effusion not rarely consists of putrid pus. Suppurative *pylephlebitis* is sometimes observed. *Thrombosis of peripheral veins* may also occur but is an unusual complication. *Infectious nephritis* occasionally supervenes and is probably due in most cases to the formation of adhesions between the appendix and the ureter. Simple *hematuria* sometimes occurs even in the absence of diffuse nephritis, as a result of renal infarction.

With operation at the present time the mortality rate for all acute cases of appendicitis is about 5 per cent., and in well-equipped hospitals under experienced surgeons it is less than this. With operation before the occurrence of peritonitis the mortality rate is less than one per cent. Appendicitis is made more dangerous by pregnancy; severe attacks frequently lead to miscarriage and not rarely to death of the fetus *in utero*.

**Treatment.**—As no one can foretell the outcome of an attack of appendicitis once it has begun, as the mortality with early operation is much lower than with any other form of treatment, operation should always be recommended as soon as the diagnosis is made, unless the services of an operator with the requisite skill cannot be secured, unless proper facilities for operating are not at hand, or unless the patient has some additional ailment that would make medical or expectant treatment seem the more safe procedure. On the whole, the best results are secured by a close coöperation of internist and surgeon. The chief aim of medical treatment is to quiet peristalsis and thus hinder the spread of the infection. From the first appearance of suggestive symptoms the patient should be at complete rest in bed, with an ice-bag over the abdomen to relieve pain. No food whatever, and no water or ice, should be given by the mouth. Enteroclysis by the drop method may be employed, however, to relieve thirst. Aperients, even the mildest, are absolutely contra-indicated. Nausea or vomiting is best controlled by washing out the stomach. Morphin as an analgesic is undesirable, as it tends to mask the symptoms. It may be given, of course, in accordance with the indications, when operation is refused or for some reason cannot be recommended.

Otherwise it should be given only in minimal doses after the diagnosis has been definitely made, or pending an operation.

If the patient is not seen within the first forty-eight hours and already presents the symptoms of diffuse peritoneal infection and toxemia—frequent pulse (130–140), high temperature (102°–103° F.) pinched features, cyanosis, extreme abdominal distention, diffuse tenderness and rigidity, intestinal paresis, etc.—it is probably better not to open the abdomen at once, but to wait for localization of the process, following in the meantime the plan of treatment suggested by Ochsner to control peristalsis and favor limitation of the infection. Some surgeons, however, believe that more lives are saved by making a simple incision, thus relieving the tension and affording exit to the infected exudation. Briefly stated, Ochsner's treatment consists in maintaining the Fowler position, washing out the stomach, withholding food, water and all medicines by the mouth, applying heat or cold to the abdomen, and giving saline solution freely by the rectum, and, if necessary, also by subcutaneous injection.

## CHRONIC APPENDICITIS

Chronic appendicitis usually supervenes upon the acute form, but it may be chronic from the beginning. The condition is characterized by connective-tissue hyperplasia with erosion or scarring of the mucous membrane and consequent thickening of the appendix and more or less obstruction of its lumen. Adhesions are almost always present. When obliteration of the lumen is limited to the proximal end of the appendix the rest of the organ may be transformed into a retention-cyst. Occasionally such cysts reach a large size and in their jelly-like contents (pseudomyxomatous cysts) resemble colloid carcinomata.

**Symptoms.**—Chronic appendicitis is usually characterized by intractable, but capricious, dyspeptic phenomena, more or less discomfort in the region of the appendix, and frequent or infrequent acute attacks, some of which may be mild and ill-defined (chronic relapsing appendicitis). More rarely there are recurring acute attacks of more or less severity without any local or general abdominal symptoms in the intervals. In another group of cases the disturbances are chiefly gastric or intestinal, there being no definite attacks and but few symptoms directly referable to the appendix (chronic, masked or larval appendicitis). When the chief symptoms are referred to the digestive organs the resemblance to peptic ulcer, on the one hand, or to chronic cholecystitis on the other, may be very close, although it is usually possible to detect certain discrepancies in the clinical picture. Dull pain in the right iliac region is a common manifestation, and both this and the epigastric discomfort are likely to be increased by physical exertion. The large majority of patients complain of constipation, but there may be diarrhea, or the two conditions may alternate. Occasionally mucous colitis supervenes. A slight daily rise of temperature persisting for weeks is sometimes observed. The general health is often more or less affected, and in exceptional instances chronic appendicitis is the primary condition underlying secondary neurasthenia. Occasionally, too, the focus of infection responsible for chronic arthritis is in the appendix.

Physical examination of the abdomen shows in many cases some tenderness over McBurney's point, and exceptionally a palpable appendix. Bastedo's sign—the occurrence of pain and tenderness over McBurney's point

upon distention of the colon with air—is often present, but it is not very characteristic. Occasionally there is a visible swelling in the right flank from a gas-filled cecum—the so-called "air-cushion" symptom. The roentgen ray may show intestinal stasis, spasticity of the colon, abnormal retention of the opaque meal, kinking or malposition of the organ, and even shadows of concretions, but these signs are not altogether reliable. Nevertheless in doubtful cases radiographic studies are often of great value in excluding other conditions, such as peptic ulcer, cholelithiasis, renal calculus, etc., which may simulate chronic appendicitis.

**Diagnosis.**—The recognition of chronic appendicitis presents many difficulties, but usually a minute history and a thorough physical examination, including radiographic studies, will lead to a correct decision. Among the conditions that are likely to cause confusion may be mentioned so-called nervous dyspepsia, peptic ulcer, chronic cholecystitis, with or without gall-stones, renal or ureteral calculus, loose right kidney, an infected ectopic kidney, disease of the right Fallopian tube or ovary, visceral ptosis, mucous colitis, pericolic adhesions with intestinal stasis, and abnormality mobility of the cecum. Carcinoma of the appendix and hyperplastic ileo-cecal tuberculosis commonly produce an identical clinical picture, although the latter should be strongly suspected if a distinct swelling of comparatively long duration is present in the cecal region and there are signs of pulmonary consolidation with fever, sweating and emaciation.

**Treatment.**—The treatment of chronic appendicitis is wholly surgical, but operation should not be urged unless the diagnosis is reasonably certain. The removal of the appendix for the relief of symptoms that point equivocally to several organs, including the appendix, must of necessity often prove ineffectual. Good results may be expected from appendectomy, however, in almost all cases in which there is definite history of acute appendicitis.

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## DIVERTICULA OF THE INTESTINES

Diverticula or pouchings of the intestines may be congenital or acquired, and according to structure, true or false. True diverticula are composed of all the coats of the normal bowel; false diverticula are herniaform protrusions of the inner coats through the muscularis. The latter variety is the more common. Meckel's diverticulum is the most important example of a congenital true diverticulum. It occurs in from 0.5 to 2 per cent. of all persons (Kelly and Hurdon), and usually arises from the ileum within a meter (39.3 inches) of the cecum. Acquired diverticula may occur anywhere in the intestines from the pylorus to the anal ring, even the appendix itself not escaping. The sigmoid flexure, however, is the favorite site. They are usually multiple, and when in the small bowel are almost always along the line of the mesentery. Their origin is still a mooted question, but it is generally believed that a local defect exists in the intestinal wall and that the weak point yields under the pressure of gas and feces. Traction appears to be an unimportant factor. Of diverticula giving rise to symptoms the large majority are in adults, and more than two-thirds are in males. Obesity is undoubtedly a predisposing influence.

Although harmless in themselves, diverticula, like the appendix, are a potential source of danger. Meckel's diverticulum, especially if its distal end is attached, may ensnare the bowel in various ways and cause constriction and strangulation. When the distal end is free invagination sometimes

occurs, usually in association with invagination of the bowel, and occasionally a floating diverticulum becomes twisted upon itself. With these exceptions, diverticula become dangerous chiefly through the secondary changes that may occur within them. Inflammation—diverticulitis—is the most common secondary change. It is analogous to appendicitis from the points of view both of its etiology and pathology. The lesions, however, are for the most part extramucosal and rarely proceed to gangrene. The symptoms of diverticulitis also resemble those of appendicitis, but the local phenomena—pain, tenderness, tumor, etc.—are far more frequently formed in the left lower quadrant of the abdomen than in the right lower quadrant. The process may be acute, persist for a few days, and then entirely disappear. Recurrences, however, are the rule. Perforation, resulting in localized abscess or more rarely in diffuse peritonitis, sometimes occurs. The abscess may rupture into the bowel, but more frequently it breaks into the bladder, forming a vesico-colic fistula. Obstruction of the intestine sometimes ensues owing to occlusion of the bowel by the inflammatory mass, to compression by adhesions, to kinks or to paralysis of peristalsis.

In many cases the inflammation is of the subacute or chronic type and is characterized by the appearance of a mass, usually in the left lower quadrant of the abdomen, and recurring attacks of pain, with fever and constipation. The condition may readily be mistaken for pelvic inflammatory disease, retroperitoneal abscess, left-sided appendicitis, and especially carcinoma of the sigmoid flexure. In carcinoma, however, the course is more uniformly progressive, the general nutrition is usually not so well maintained, blood is frequently found in the stools, local pain is a less prominent feature, and sigmoidososcopic examination not rarely shows an actual tumor. Roentgen findings may be helpful in diagnosis, but they are likely to be equivocal. The difficulty in differentiation is increased by the fact that carcinomatous degeneration frequently follows diverticulitis. Carcinoma coexisted in 13 of 42 cases (30.9 per cent.) treated surgically at the Mayo clinic.[1]

## CHRONIC CONSTIPATION

**(Intestinal Stasis; Obstipation; Costiveness)**

**Definition.**—Constipation is a condition in which the feces are retained in the intestinal canal an abnormally long time, with the result, as a rule, that the stools become unduly inspissated and are passed less frequently than usual.

Even in health the frequency of defecation and the amount and consistence of the feces are subject to considerable variation. Many persons who appear normal evacuate the bowels twice a day; others again, who seem equally well, defecate but once every two or three days, and cases are on record in which the interval between successive evacuations has been regularly two or three weeks, and this without any local or constitutional disturbance. As a general rule, however, persons in good health have an action of the bowels once in twenty-four hours, and, if the conditions of life are uniform, usually at about the same time of day.

**Etiology.**—Normally, the passage of chyme through the small intestine is fairly rapid, the cecum being reached by opaque ingesta in a little over four hours. The contents of the large intestine, on the other hand, are driven forward much more slowly, about twelve hours being required for barium-

[1] Jour. Amer. Med. Assoc., Sept. 8, 1917.

ized food to pass from the cecum to the pelvic colon (sigmoid), and another eight hours usually elapsing before evacuation occurs. Consequently, the passage of food from the mouth to the anus ordinarily occupies in all from 25 to 30 hours. Under normal conditions the feces do not pass beyond the pelvi-rectal flexure until immediately before defecation, but accumulate from below upward in the pelvic colon. When the latter is sufficiently distended, an increase of peristalsis occurs forcing the fecal mass into the rectum, where it produces the peculiar sensation calling forth the desire to defecate. The evacuation of the feces is then accomplished partly by a voluntary contraction of the abdominal muscles, which forces more fecal matter into the rectum, and partly by reflex stimulation from the lumbar spinal cord, which still further increases colonic peristalsis and also causes relaxation of the sphincters. Normally, defecation completely evacuates all the contents of the bowel beyond the splenic flexure.

The chief factor in the propulsion of the feces through the colon is probably the mass movement first described by Holzknecht. This is a sudden powerful contraction of the bowel that rapidly pushes forward the entire fecal mass, the distance travelled varying with the circumstances. The movement occurs at intervals, probably about six times daily, and is strongest after breakfast when food is received in the stomach after a night's fast.

The causes immediately responsible for constipation are (1) diminished expulsive power, (2) decreased irritability of the intestine, (3) lack of the normal stimulus to defecation, and (4) increased resistance to the onward movement of the feces. In many cases more than one of these causes is operative.

Senility, cachexia, anemia and acute fevers all tend to produce constipation by weakening the intestinal musculature. Sedentary habits are potential in the same way. Persons with splanchnoptosis are especially prone to coprastasis, owing to atony of the abdominal muscles or, less frequently, to kinking or angulation of the bowel. In some instances the voluntary contractions of the abdominal muscles, which normally assist in the act of defecation by increasing the intra-abdominal pressure, are rendered inefficient by defects in the pelvic floor that have been produced by a difficult labor. In other cases, the important factor is atony of the abdominal wall brought on by overdistention of the abdomen, as from repeated pregnancies, obesity, ascites, etc., or weakness of the muscles of the intestines themselves from overstretching of the bowel by gas or feces.

The influence of the central nervous system over intestinal motility is shown by the frequency of costiveness in certain functional nervous disorders, such as neurasthenia and hysteria, in the psychoses, especially melancholia, as well as in many organic diseases of the brain and spinal cord. Peristalsis may also be slowed by irritation of the sympathetic nerves arising from various painful abdominal conditions, such as chronic appendicitis, oöphoritis, cholelithiasis and peptic ulcer, although it must be recognized that painful impulses and many abnormal nervous influences, instead of stimulating the sympathetic system, may affect the augmentor fibers of the vagus and thus excite a tonic spasm of the bowel, the effect of which is to hinder the onward movement of the feces.

The habit of resisting the call to defecation owing to lack of time, false modesty, or fear of pain, as in cases of anal fissure, is another potent factor in producing constipation. It operates by blunting the sensitiveness of rectal mucous membrane, normal stimuli in consequence becoming less effective. In a similar manner the repeated use of strong purgatives may also weaken the defecation reflex. Passive congestion of the bowel, the

result of chronic heart or liver disease, and chronic intestinal catarrh not infrequently cause constipation by diminishing the sensitiveness of the intestines or by reducing the strength of the expulsive movements.

Constipation is very often due to dietetic errors, an insufficient amount of food being taken, or the food being too concentrated or containing too little indigestible matter (cellulose, muscle fibers, etc.) to stimulate peristalsis. Undue inspissation of the intestinal contents may also result from the insufficient use of water or from an excessive loss of water, as in persistent vomiting or habitual polyuria. According to Schmidt[1] and Strassburger,[2] sluggishness of the bowels frequently depends upon a too complete digestion and utilization of the ingested food, not enough nutrient residue remaining to support the bacteria which produce the necessary stimulant of peristalsis (acids and gases). Gastric disorders are sometimes directly responsible for intestinal stasis, but the exact manner in which they affect the bowel is not always clear.

Many cases of obstinate constipation depend upon increased resistance to the onward movement of the intestinal contents. This may be due to (a) abnormal hardness or dryness of the feces; (b) fecal accumulation brought on by constipation from other causes; or (c) narrowing of the lumen of the bowel itself, the consequence of various organic conditions or of spasm. Organic obstruction may be caused by kinks or angulations, the result of adhesions, evolutionary bands, visceroptosis, etc., by strictures or congenital malformations, or by the pressure of tumors or of other organs. Enterospasm (spastic constipation) is especially common in hysteria and neurasthenia, but it is also frequently observed as a reflex phenomenon depending upon chronic appendicitis, chronic cholecystitis, ovarian disease, hemorrhoids, anal fissure, etc. An extreme form is observed in chronic lead poisoning. In some instances spasticity of the descending colon is associated with atony or dilatation of the ascending colon (dyskinetic constipation).

**Symptoms.**—Simple constipation is not necessarily a cause of poor health, and is often manifested only by infrequent evacuation of the bowels. In many cases, however, retention of the feces beyond the usual period is accompanied not only by certain abdominal symptoms, such as a sense of fulness, flatulence, attacks of colicky pain, and a feeling of discomfort in the rectum, but also by some degree of general disturbance, indicated by mental sluggishness, depression of spirits, dull headache, a tendency to dizziness, fetor of breath, a coated tongue, and impairment of appetite. In long-standing cases more pronounced nervous conditions, such as neurasthenia, psychasthenia, and hypochondriasis, are sometimes present, and occasionally the general nutrition is much impaired, as shown by anemia, weakness and emaciation. In rare instances acute febrile attacks may also occur. These symptoms are usually attributed to the absorption of poisons derived from the decomposition of certain foods (intestinal toxemia), although the evidence in favor of this view does not amount to actual proof. In some cases the symptoms are better explained on the basis of a mild infection (subinfection) of intestinal origin, which has become effective by breaking down of the natural protective agencies existing in the bowel itself and other organs. In other cases the general disturbances appear to be the cause of the intestinal torpor rather than its effect.

In addition to producing the symptoms already mentioned, habitual constipation may favor the occurrence of other disorders of various sorts. That it has a contributing causal relation to certain skin diseases, such as acne and

[1] Münch. med. Woch., 1905, No. 46.
[2] Ztschr. f. klin. Med., 1902, 46.

eczema, is well recognized. Reference has frequently been made to the association of so-called hyperchlorhydria and constipation, although the sequence of these two conditions is probably not always the same. Some authors believe that chronic arthitis is sometimes due to intestinal stasis with consequent toxemia or infection. It is a matter of common experience also that the symptoms of advanced cardiac, renal and hepatic disease are aggravated by constipation. Finally, in rare instances fecal stagnation is accompanied by the formation of large quantities of hydrogen sulphid, which by producing sulph-hemoglobinemia cause persistent cyanosis (enterogenous cyanosis).

The mechanical effects of accumulated feces are often important. Hard excrement may irritate the bowel and excite a continuous diarrhea, the liquid material passing through or around the impacted fecal mass. In other cases despite a daily evacuation of the bowels, hard foul-smelling masses are occasionally discharged. Mucous colitis is not rarely found in association with intestinal stasis, either as cause or effect. The impaction of feces in the rectum may give rise to local pain, with tenesmus and the passage of blood, and may also lead to the development of hemorrhoids. Impaction of feces elsewhere in the large bowel is sometimes followed by ulceration, which in healing may produce cicatricial contraction or stenosis. The perforation of a stercoral ulcer has also been known to occur. Fecal accumulations are sometimes palpable through the abdominal wall and may simulate various abdominal tumors. Such masses, however, are usually moveable and have a doughy feel, are only slightly sensitive to touch, and, as a rule, disappear after purgation or the use of enemata. Occasionally, hardened scybala give rise to acute intestinal obstruction, either directly or by becoming infiltrated with salts of calcium or magnesium and forming enteroliths.

Patients with spastic constipation are usually of a neurotic type and not rarely suffer also from pylorospasm and so-called hyperchlorhydria or from mucous colitis. The colon itself is sometimes tender, and in extreme cases may occasionally be felt as a tense cord. The anal sphincter is often contracted and in many cases the stools are in the form of spherical masses or are narrow and pencil-like. In rare instances persistent spasm of a segment of the bowel is followed by symptoms of acute intestinal obstruction—Leube's "ileus spasticus."

The recognition of constipation is not likely to prove difficult, especially if one bears in mind that it is not of necessity a condition of infrequent defecation. In doubtful cases delay in the passage of the intestinal contents may be shown by administering charcoal and noting the time required for its complete evacuation. Normally, it should be evacuated within forty hours. Fluoroscopy usually aids materially in determining the immediate cause of intestinal stasis and also the exact situation in which the fecal current is delayed. In constipation not due to organic conditions the arrest is usually in the sigmoid and rectum or in the cecum. Stasis in the rectum (*dyschezia*) is readily revealed by the presence of considerable quantities of feces just within the anus at any period except immediately before defecation. It has been shown that stasis in the distal colon or rectum is more likely to be associated with constitutional disturbances than that occurring in the cecum.

**Treatment.**—Although certain remedial measures are applicable to many cases of constipation, no method of treatment can be entirely satisfactory that does not take into consideration the causal factor and effect its removal. In constipation due to atony of the bowel foods that yield much undigested residue are indicated, provided, of course, that they do not disturb digestion.

Thus, vegetables rich in cellulose, such as lettuce, celery, spinach, string beans and tomatoes, and farinaceous foods containing the hulls of grain, such as graham and whole wheat bread, and oatmeal gruel or crackers, should be given. Fruits and nuts, if well borne by the stomach, are especially useful. In mild cases a few English walnuts after dinner or an orange before breakfast may supply the necessary stimulus to peristalsis. Fats and oils form soaps, which are laxative and, if well received by the stomach, may have a very useful effect, particularly if the patient's general nutrition is poor. While a certain amount of water is necessary, an excess is more likely to be diuretic than laxative, unless it is held in the bowel by a salt difficult of absorption (Epsom or Rochelle salt) or by some inert substance which readily swells in water (agar-agar). In a small percentage of cases even half a dram (2.0 gm.) of Epsom salt taken in a glass of water before breakfast is effective. Agar-agar (2–6 teaspoonfuls daily) may be served in broths, gruels, or cooked fruits, or may be taken dry and washed down with fluid.

The cultivation of regular habits in regard to defecation is of prime importance and therefore the patient should be instructed to make a determined effort to have a bowel movement once daily, always at the same hour, preferably in the morning after breakfast, even if there is no desire at the time or whether a result is obtained or not. At first the effort will have to be supplemented by the use of a glycerin or soap suppository, or a small enema of normal saline solution, but gradually these aids should be withdrawn.

For patients with relaxed and weakened abdominal muscles systematic exercise in the open air, if possible, or indoors, if necessary, is indispensable. Massage, if correctly given over a long period of time, is also of service. In mild cases self-massage may be practised by kneading the abdominal muscles in the direction of the colon or by rolling over the abdomen in the same direction a cannon-ball (3 or 4 pounds) covered with chamois-skin. Hydrotherapy, especially in the form of cold abdominal compresses or the abdominal douche with hot and cold water alternately (so-called Scotch douche) is a valuable addition to physical exercise. Patients with visceroptosis or a large pendulous abdominal wall should wear a suitable belt, and this should be applied before rising in the morning and not removed until bedtime.

When the stasis is mainly in the pelvic colon or rectum (dyschezia) enemas of plain water, soap and water, or normal saline solution are preferable to cathartics by the mouth. Injections of warm black coffee are sometimes very effective. Glycerin (a teaspoonful) is also efficacious. For occasional use, when it is necessary to empty the bowel quickly, the following compound enema will be found efficient:

℞. Magnesii sulphatis..... ℥ii (60.0 gm.)
Olei terebinthinæ..... f℥ss (15.0 mils)
Glycerini..... f℥i (30.0 mils)
Aquæ.....q. s. ad f℥iv (120.0 mils) M.

In the milder cases of constipation suppositories of glycerin, soap or gluten may suffice. Neither enemas nor suppositories should be used continuously for long periods, for in time they render the bowel less responsive to natural stimuli. If there is fecal impaction, if hard scybala occur in the stools, or if there is abnormal secretion of mucus, injections of warm cottonseed oil (100° F.) may often be used with advantage. The oil is best given at bedtime and allowed to remain in the bowel over night. It should be introduced slowly while the patient is on the back with the hips raised. From 4 to 6 ounces (120.0–180.0 mils) may be injected every two or three days. If necessary the injection of oil may be followed by one of plain water. Hard fecal masses in the rectum may also be softened by enemas containing

ox-gall (2 drams—8.0 gm.) to the pint (0.5 L.) of water. Very hard collections must sometimes be broken up by the gloved finger or a blunt instrument before they can be evacuated by enemas.

Irrigation of the colon at intervals of two or three days sometimes yields very good results in the cases of stasis in which obscure cerebral symptoms are present or in which hard, foul-smelling masses are occasionally passed. The rectum and sigmoid should first be emptied by an enema and then 2 or 3 pints of warm normal salt solution should be allowed to flow in and out of the bowel through a soft rubber colon tube while the patient lies on the left side, with the knees drawn up, and with the abdomen as relaxed as possible. The reservoir should be held at a height of about 2 feet and the tube should be introduced for a distance of 6 inches, backward and forward movements being constantly made so as to permit the escape of any gas that may be present.

Dietetic and physical treatment will not cure all cases of constipation and the administration of drugs often becomes a necessity. For habitual use the anthracene cathartics—cascara, aloes, rhubarb, senna, and phenolphthalein—are usually chosen. A sufficient dose should be employed to secure a satisfactory movement, but it is important to avoid active purgation. As a rule, a combination of two or three drugs is more effective than a single drug. Nux vomica or physostigma is often added to the combination to enhance its stimulating effect, and belladonna to prevent griping. Ordinarily, vegetable laxatives cause less inconvenience when taken at bedtime or after the evening meal. Sometimes, however, better results are obtained by giving small doses after each meal. Such combinations as the following often prove satisfactory:

℞. Extracti cascaræ sagradæ..... gr. xlviii (3.1 gm.)
Aloini.....
Extracti nucis vomicæ.....āā gr. iv (0.25 gm.)
Extracti belladonnæ..... gr. iii (0.2 gm.) M.
Misce et fiant pilulæ No. xxiv.
Sig.—One pill at bedtime.

℞. Extracti cascaræ sagradæ..... gr. xl (2.5 gm.)
Resinæ podophylli..... gr. iii (0.2 gm.)
Extracti colocynthidis compositi..... gr. xxx (2.0 gm.)
Extracti physostigmatis..... gr. iv (0.25 gm.)
Extracti hyoscyami..... gr. x (0.65 gm.) M.
Misce et fiant pilulæ No. xx.
Sig.—One pill night and morning.

In some cases of constipation, especially if gout, diabetes or chronic gastric catarrh is also present, salines are preferable to vegetable cathartics. One of the natural mineral waters, such as Hunyadi, Apenta, Bedford or Saratoga may be employed, although equally good results may be obtained from 1 or 2 drams (4.0–8.0 gm.) of Rochelle salt, magnesium sulphate, or sodium phosphate, taken before breakfast or at night in a glass of hot or cold water. In conjunction with enemas and careful abdominal manipulation, salines, in small doses at short intervals, are also the cathartics of choice in fecal impaction. In the cases in which gastric hyperacidity accompanies constipation magnesium oxide is especially valuable. Castor oil and calomel are not suitable for continuous use, but are often very serviceable in acute exacerbations. When the stools are dry, or the constipation is the result of enterospasm or of partial obstruction, or is accompanied by mucous colitis, pure liquid petrolatum is frequently of value. From ½ to 1 ounce (15.0–30.0 mils), with cold water or orangeade, should be taken at night or two or three

times a day between meals, that is when the stomach is empty. It is sometimes necessary to add a small amount of cascara to secure the best results.

In spastic constipation general massage is sometimes useful, but all local stimulation must be forbidden. Periods of absolute rest are often imperative. Warm abdominal compresses are efficacious, especially when there is much colicky pain. Harsh, irritant foods are harmful. Injections of a few ounces of warm oil every night or every other night are of great value. By the mouth, liquid petrolatum and agar-agar are worthy of trial. Atropin, beginning with $\frac{1}{100}$ of a grain (0.00065 gm.) twice a day, and gradually increasing the dose until physiologic effects are produced, is sometimes successful. A glass of hot water night and morning also tends to relax the spasm of the bowel. From time to time moderate doses of castor oil to which a few drops of laudanum have been added may often be used with advantage. Dilatation of the sphincter has been tried with varying success.

*Surgical Treatment.*—In certain well chosen cases of chronic constipation good results may sometimes be obtained by surgical treatment. The most important measures are suspension of the colon, partial or complete colectomy, and various short circuiting operations. The patients most likely to be benefited by surgical intervention are those in whom there is definite evidence of partial obstruction and who have become disabled by the condition despite protracted and varied medical treatment. Such serious measures, however, cannot be undertaken without some risk even by the most skillful and are certainly inadvisable for congenital cases presenting signs of faulty development outside of the intestinal tract or for the relief of nervous symptoms in cases of simple constipation, no matter how severe this may be.

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## IDIOPATHIC DILATATION OF THE COLON

**(Megacolon; Hirschsprung's Disease)**

Apart from the dilatation of the colon resulting from severe chronic constipation and that dependent upon obvious mechanical obstruction, there is a comparatively rare form of ectasia that arises without discoverable cause and to which the term "idiopathic" is usually applied. This form in the large majority of cases is present at birth or develops in early childhood, so that a congenital origin is probable. The nature of the abnormality, however, is not apparent. In many cases only the sigmoid flexure and the descending colon are affected, but not rarely the entire large bowel, including the cecum is involved. The size reached may be enormous, a diameter of 15 cm. (6 inches) not being uncommon. In Formad's case of the "balloon man" the colon had a circumference in places of 76 cm. (30 inches) and weighed with its contents 47 pounds. With the dilatation there is nearly always hypertrophy of the intestinal walls, probably as a compensatory development, and ulceration of the mucous membrane is often observed. The fecal matter in the colon is, as a rule, semi-liquid, and is only exceptionally dry and scybalous.

**Symptoms and Course.**—The most constant symptoms are obstinate constipation, often of an intense grade, and marked abdominal distention, chiefly tympanitic and sometimes asymmetrical. Diarrhea not rarely supervenes from time to time, and toward the close of life may be persistent. The abdominal wall is usually not tense, as in obstruction of the bowel, and yet distended intestinal coils, with peristaltic waves slowly passing through

them, may be plainly visible. In extreme cases dyspnea may be produced by pressure against the lungs and edema of the legs by pressure on the iliac veins. Attacks of intestinal obstruction, with colicky pains, vomiting and prostration, may occur at varying intervals. The general health is always affected sooner or later, although in the milder cases it may remain fairly good for a long period. Duval[1] in 30 cases found that 84 per cent. of the patients die before reaching the age of 15 years. The cause of death may be acute or chronic intestinal obstruction, acute colitis, or intercurrent disease (pneumonia). Tetany has been known to occur (Langmead).

**Treatment.**—Medical treatment is unsatisfactory. In the absence of diarrhea, massage and electricity may be tried. Daily copious injections and the use of the rectal tube to remove gas afford temporary relief. Purgatives, with the exception of liquid petrolatum, are objectionable, although it is often necessary to use them. In a number of cases surgical treatment, especially partial colectomy, has proved successful, but the mortality is high. According to Ladd[2] of 118 cases, 60 were treated medically, with 41 deaths (67 per cent.) and 7 recoveries; and 58 were treated surgically with 24 deaths (41 per cent.) and 24 recoveries. Hoffmann[3] reports 18 operative cases with a mortality of 38.8 per cent.

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## INTESTINAL OBSTRUCTION

The term intestinal obstruction is applied to any condition that seriously hinders or arrests the onward movement of the intestinal contents. Acute and chronic forms of obstruction occur, but in the chronic form the symptoms may at any time become acute. No sharp line of distinction can be drawn between chronic intestinal obstruction and ordinary constipation; indeed, the latter often depends upon chronic partial obstruction of the colon, in the form of angulations or kinks, due to coloptosis or to certain membranous bands, congenital or acquired.

**Classification.**—Generally speaking intestinal obstruction is due either to mechanical closure of the intestinal lumen—*mechanical obstruction*, or to loss of propelling power in the intestinal musculature—*dynamic obstruction*.

The chief causes of mechanical obstruction are: (1) strangulation by fibrous bands or in apertures, normal or acquired; (2) infolding of the gut into itself (invagination); (3) twist, or volvulus; (4) abnormal intestinal contents; (5) compression by tumors or cysts external to the bowel; (6) tumors of the bowel; (7) stricture or atresia.

Dynamic obstruction may be due to: (1) lesions directly affecting the intestinal musculature, such as acute peritonitis, embolism or thrombosis of the mesenteric vessels with infarction of the bowel, excessive meteorism, etc.; (2) injuries or disturbances causing a reflex inhibition of the muscular coat of the bowel, such as intra-abdominal operations, contusions of the abdomen, injury of a testicle, torsion of an ovarian cyst, passage of a renal calculus, etc., (3) toxic conditions affecting the neuromuscular mechanism of the bowel, such as occur in pneumonia and other acute infections, (4) nervous conditions affecting unfavorably the innervation of the bowel, such as certain injuries of the spinal cord and hysteria.

[1] Rev. de Chirurg., 1905, xxiii, 5.
[2] Boston Med. and Surg. Jour., Jan. 27, 1921.
[3] Deutsch. Zeitsch. f. Chir., 1921, clxi.

Both mechanical and dynamic obstruction are often present in the same case. Thus, in simple paralysis of the bowel there may be kinking due to loss of tone and in strangulation, invagination, etc., secondary peritonitis and toxemia invariably develop unless the condition is quickly relieved.

**Effects.**—Complete occlusion of the intestinal lumen, if acutely developed, results in marked changes in the bowel both below and above the obstruction. Below the obstruction the bowel is paralyzed and relaxed, and in consequence not even flatus escapes from the anus. Above the obstruction there is stagnation of the intestinal contents, with rapid multiplication of bacteria and distention of the bowel with gas. At first the distended coils contract vigorously, but in a short time the movements cease and paralysis supervenes. Even when there is no compression of the intestinal vessels from without, the wall of the bowel at the site of the obstruction sooner or later becomes necrotic and ulcerated. these changes being due in part to extreme distention of the bowel and consequent interruption of the capillary circulation and in part to bacterial invasion of the poorly nourished tissues. When the intestinal circulation is obstructed from without, as in strangulation by fibrous bands, invagination or tight twists, the nutrition of the bowel is very early affected, venous stasis, edema, hemorrhagic extravasation and necrosis occurring in rapid succession. The degenerative changes in the intestinal wall, even if they do not proceed to actual perforation, favor the escape of bacteria, and therefore peritonitis, localized or diffuse, is an important sequel in all forms of acute obstruction. As the result of a generalized infection the liver, spleen or kidneys often become congested.

Apart from complete arrest of evacuation, the most important clinical manifestations of *acute intestinal obstruction* are abdominal pain, vomiting, tympanites and collapse. The pain at first is chiefly due to the violent contractions (tonic) of the intestinal coils above the point of closure. Later, it may be the result of peritonitis. The vomiting in the early stages is clearly a reflex phenomenon; its continuance, however, probably depends in most instances upon the action of toxic products absorbed from the intestine. As a rule, the vomitus after a time consists of yellowish or brownish liquid, of a characteristic fecal odor. Whether the entrance of this stercoraceous material into the stomach is occasioned simply by an overflow of the stagnant intestinal secretions, which have accumulated above the obstruction, or is brought about by antiperistaltic movements has not been definitely determined. The tympanitic abdominal distention is to be ascribed to an overproduction of intestinal gases, to an excessive accumulation of these gases caused by failure of escape through the anus and by diminished absorptive power in the damaged bowel, and also to a loss of tonus in the intestinal musculature. The profound prostration and collapse, which are such prominent features in all acute obstructions and which in the majority of cases are the immediate cause of death, result from the absorption of certain poisons, the origin of which has not been definitely established. Whatever their source, however, it is certain that their entrance into the blood depends almost entirely upon the injury to the intestinal mucosa brought about by the obstruction. Dehydration of the tissues caused by excessive drainage into the lumen of the bowel and by vomiting may also be a factor in determining the fatal issue, but undoubtedly it is much less important than the toxemia. The graver and more acute systemic disturbance in obstructions high in the bowel, as compared with low ones, may be due to certain poisons formed in the stomach or duodenum, which under normal conditions are rendered inert in the lower portions of the intestinal canal. Draper[1] suggests

[1] Jour. Amer. Med. Assoc., Nov. 24, 1917.

that the much dreaded symptoms of complete duodeno-jejunal obstruction (tachycardia, tetanoid seizures, collapse) are a result of perverted enzymal function and the consequent production of toxic bodies that cannot be isolated by ordinary chemical analysis.

In *chronic obstruction* the intestine below the stenosis is pale, thin-walled and collapsed, and above the obstruction it is distended and, as a rule, thickened, as a result of hypertrophy of the muscular coat. The hypertrophy is due to the increased efforts of the bowel to overcome the obstruction. Immediately above the constriction the mucous membrane often shows extensive ulceration, the result of overdistention of the intestine and the irritant action of retained contents. Not rarely in chronic obstruction acute symptoms supervene owing to the contracted lumen becoming completely blocked by masses of hardened feces.

**Symptoms.** *Acute Obstruction.*—Pain is usually an initial symptom. As a rule, it is sudden and severe and colicky in character, although after a time it often becomes more or less continuous. It may be localized to a particular spot, but more frequently it is diffuse. Soon after the onset, often within a few hours, vomiting sets in and continues with ever increasing frequency. The vomit at first consists of the contents of the stomach, then of bile-stained mucus and eventually of brownish or yellowish fluid of an unmistakable fecal odor. The rarity of true stercoraceous vomiting in other conditions makes this feature especially important. Absence of bowel evacuations is a cardinal symptom, though frequently some time must elapse before its significance becomes apparent. Occasionally at the onset, the bowel below the obstruction is emptied, either spontaneously or in response to an enema, but as a rule constipation is absolute from the beginning, even the escape of flatus being arrested. Tympanites appears in almost all cases and is usually pronounced, although it may be slight if the obstruction is high up in the small bowel. Until the peritoneum becomes involved there is rarely any marked tenderness or muscular rigidity. In many cases peristaltic movements are plainly visible through the abdominal wall and are very characteristic of obstruction. In the later stages, after the bowel has become paralyzed as a result of over-distention or peritonitis, all peristaltic movements and sounds cease. The constitutional disturbance, generally speaking, appears earlier and is more severe in proportion to the nearness of the seat of obstruction to the stomach. Prostration, however, always sets in soon after the onset, and in the majority of cases collapse ensues within a few days. The pulse is unchanged at first, but with the occurrence of peritonitis and collapse it becomes rapid and feeble. The temperature, too, is usually normal until peritonitis develops. Leucocytosis is generally present unless there is grave intoxication. The urine is scanty, is often slightly albuminous, and may contain an excess of indican. A pronounced increase in the non-protein and urea nitrogen of the blood is usually observed even in the absence of nephritis (Tileston and Comfort, Whipple and Van Slyke, Louria). Unless relief is promptly afforded the patient succumbs within a week or ten days, and not rarely within 48 hours. In the terminal stage the face is pale and bathed in cold sweat, the features are pinched, the eyes are sunken, and finally stupor or coma supervenes.

*Chronic Obstruction.*—The first indication of chronic intestinal obstruction is usually a disturbance in defecation. In the great majority of cases there is increasing constipation with recurring attacks of colicky pain and abdominal distention. The occurrence of visible or of palpable peristaltic waves during such attacks is very significant. The stools often consist of small ball-shaped masses, resembling sheep's dung, or are pencil-shaped or

flat and tape-like, but these changes in form are not of themselves characteristic of organic stenosis, as they may also be seen in simple spastic constipation. Although constipation is the rule, attacks of diarrhea not rarely occur from time to time, and in exceptional cases the stools may be loose throughout the entire course of the disease, the cause of these anomalies being the development of an inflammatory conditon in the bowel above the stenosis. With the increasing obstruction, there may be a gradual enlargement of the abdomen from tympanites, and careful examination may show that certain loops of intestine are especially distended and the seat of paroxysmal tetanic contractions—an observation of prime importance in the diagnosis. In many cases hard masses may also be detected by abdominal palpation or by digital examination through the rectum. Symptoms of acute obstruction may set in at any time, the narrow lumen of the bowel becoming blocked by hardened feces; otherwise vomiting and constitutional symptoms are rarely marked until a late stage has been reached. In irremediable cases death results from supervening acute obstruction, asthenia, or peritonitis following perforation of the bowel above the point of obstruction.

**Special Features.**—Strangulation, invagination, volvulus, foreign bodies, and paralysis of the bowel, due to abdominal operations, acute peritonitis, etc., usually lead to acute obstruction. On the other hand, tumors and cicatricial strictures of the bowel, compression of the bowel from without, and fecal accumulations usually give rise to chronic obstruction.

*Strangulation.*—Excluding intestinal constriction in external hernias, so-called internal strangulation constitutes by far the largest proportion of cases of intestinal obstruction. Some part of the small intestine is usually involved, and the most common site of the lesion is in the right lower quadrant of the abdomen. Adhesions, the result of previous attacks of peritonitis, are the chief causes of internal strangulation. Next in etiologic importance is Meckel's diverticulum, the distal end of which is frequently attached to the mesentery, umbilicus, or small intestine by a fibrous cord. Occasionally, the bowel is caught under an anomalous band uniting the appendix vermiformis, a Fallopian tube or an appendix epiploica with some other intra-abdominal structure. A comparatively uncommon form of strangulation is that caused by the passage of the bowel through a slit (congenital or acquired) in the mesentery or omentum, and equally uncommon is that form caused by the protrusion of the bowel into a subperitoneal or retroperitoneal fossa or pouch (internal hernia). Worthy of special mention among the internal hernias are hernia of the duodenojejunal fossa, hernias of the retrocecal or pericecal pouches, hernia of Winslow's foramen, and the diaphragmatic hernias.

The clinical picture of internal strangulation is that of acute intestinal obstruction in general and rarely portrays the peculiar lesion. A history of previous peritonitis, in particular of peritonitis following appendicitis or salpingitis, is however, suggestive of strangulation. In diaphragmatic hernias signs simulating those of pneumothorax are often present and roentgen examination yields valuable information.

*Invagination, or intussusception,* is the infolding (telescoping) of one portion of the bowel into an adjoining portion. It is the most common form of intestinal obstruction in young children and one of the most uncommon in adults. Many cases (more than 50 per cent.) occur during the first year of life. In childhood more than two-thirds of the cases are in males. It is not definitely known how the condition is produced, but it is supposed that as a result of irregular peristalsis, a tetanically contracted segment of bowel

becomes overlapped by a partially quiescent segment. In a minority of cases a polypoid tumor of the bowel or a congenital abnormality of the bowel or mesentery is to be held responsible for the process. The exciting cause is usually not apparent, but in some instances there is a history of dietetic errors, active purgation, or violent jolting. According to their location invaginations are classified as enteric (jejunal or ileal), ileocecal, or colic. In rare instances the lower part of the ileum passes through the ileocecal valve, producing a so-called ileocolic invagination. The ileocecal form, the one in which the ileocecal valve prolapses into the cecum and drags with it the ileum and its mesentery, is by far the most common, especially in childhood. The infolding of the bowel is almost invariably from above downward, ascending or retrograde invaginations being extremely rare. Occasionally two or more intussusceptions occur in the same patient. The affected segments of bowel form an elongated tumor, which on section is found to consist of three layers: an outermost or ensheathing layer (*intussuscipiens*), a middle or returning layer, and an innermost or entering layer. The innermost and middle layers together are known as the *intussusceptum*. Occasionally the ensheathing layer becomes folded upon itself producing what is termed a double intussusception. The length of bowel affected varies from a few centimeters to half a meter or more. As a result of compression of the mesenteric vessels, intense engorgement of the invaginated portion occurs and is soon followed by inflammation and agglutination of the intestinal layers or, if the circulation is completely interrupted, by hemorrhagic infarction and gangrene. The condition almost invariably terminates in fatal collapse unless appropriate treatment is promptly instituted; although cure without intervention of any kind is possible, either by spontaneous reduction of the intussusception, which doubtless occurs sometimes in mild and unrecognized cases, or, very rarely, by gangrenous separation of the intussusceptum after a complete union has been effected between the apposed serous surfaces at the upper end of the invagination.

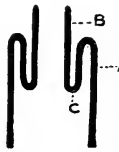

FIG. 15.—A, Intussuscipiens; B, entering layer; C, intussusceptum.

The symptoms of intussusception are usually those of acute intestinal obstruction to which are added, in a large proportion of cases, a tumor in the abdomen, commonly sausage-shaped and varying much in size and situation, the passage of blood and mucus from the anus, and tenesmus. Occasionally, the invaginated bowel can be felt in the rectum. Tympanites is not constant and the vomiting is not often feculent. In some instances, especially in adults, the disease runs a chronic course and presents a clinical picture similar to that of stricture of the bowel.

*Volvulus.*—This term is applied to twisting or rotation of a segment of intestine around its mesenteric axis, its own longitudinal axis, or an axis composed of another intestinal coil and its mesentery. The condition is more frequent in males than in females, and is much more common in persons past 40 than in the young. It most often involves the sigmoid flexure, but it may occur in the cecum or in some portion of the small intestine. The chief predisposing cause of volvulus is abnormal length of the mesentery, the elongation being either congenital or acquired as the result of fecal accumulations in the bowel, adhesions, fixation of an intestinal loop in a hernial sac, or loss of abdominal fat. The determining cause may be active purgation, violent exertion or trauma. If the twist is tight enough to arrest the circulation, changes occur in the bowel similar to those produced by strangulation. The symptoms of volvulus are those common to all forms of acute intestinal

obstruction and usually appear with extreme suddenness. Tympanites develops rapidly, as a rule, and is very pronounced. Especially significant in the early stage is the occurrence of localized tympanites, the affected loops of bowel forming a tense elastic swelling. Vomiting is not constantly present in volvulus of the sigmoid flexure, and when it does occur it is not usually feculent. Occasionally there is tenesmus with mucous and bloody discharges. Spontaneous reduction may rarely occur if the rotation of the bowel is not more than 180°.

*Abnormal Contents.*—Among the abnormal contents that sometimes cause intestinal obstruction may be mentioned masses of inspissated fecal matter, gall-stones, various foreign bodies introduced into the bowel by way of the mouth or the anus, enteroliths formed by the deposition of calcium and magnesium phosphates about hardened feces, hair, indigestible food remnants, etc., intestinal calculi composed of magnesia, chalk, salol, etc., taken as medicine for a long period of time, and collections of tangled round worms. Intestinal obstruction due to the abnormal contents may be acute or chronic. Enteroliths and fecal masses usually produce a slowly progressive stenosis of the bowel, although symptoms of acute occlusion often suddenly supervene. Ulceration of the intestine may ensue if the concretion or foreign body remains too long in one place.

Intestinal obstruction due to gall-stones is comparatively rare. It is much more frequent in women than in men (about 75 per cent. of the cases) and usually occurs in persons more than 50 years of age. The most common site of the obstruction is the ileum at or near the ileocecal valve. In some instances there is no history pointing to cholelithiasis. Both the existence and the approximate localization of foreign bodies, concretions, etc. are frequently revealed by the x-ray.

Fecal impaction is relatively common and usually occurs in the rectum and sigmoid or in the cecum. The symptoms develop, as a rule, in a gradual manner, but they may become acute at any time. Moreover, partial occlusion of the bowel, the result of tumor or stricture, may be made complete by fecal accumulation. There is usually a history of antecedent constipation and not rarely palpation through the abdominal wall reveals a nodular mass which when firmly pressed becomes altered in form. Sometimes the mass becomes hollow in the center and thus permits the passage of fluid feces.

*Compression by Tumors, etc.*—Intestinal obstruction is sometimes the result of compression of the bowel by tumors, cysts, abscesses, displaced organs, etc. The rectum and sigmoid flexure are the parts of the bowel most frequently affected, and tumors of the ovaries and uterus are the most common causes of compression. In some instances elongated adhesions compress the bowel sufficiently to narrow its lumen but do not exert enough pressure to interfere with its circulation (strangulation). A subacute form of obstruction due to adhesions is not rarely observed in fibroplastic tuberculous peritonitis. The symptoms of compression are usually those of chronic obstruction, although after a time they often become acute. Even when acute, however, they are less severe, as a rule, than those resulting from strangulation.

*Tumors of the Bowel.*—Of all intestinal tumors, malignant or benign, carcinoma is by far the commonest, and the one usually responsible for stenosis (for details see p. 486). The rectum and colon are the parts most frequently involved. Symptoms of gradually developing intestinal obstruction—increasing constipation, or alternating constipation and diarrhea, colicky pains, meteorism, etc.—are usually present. In addition, a tumor can frequently be palpated through the abdominal wall as a firm, slightly

tender, and rather freely moveable mass, or can be detected without difficulty by a rectal examination. Localized pain usually appears sooner or later. In some instances it radiates to the back, to the thighs, or to the genitals. In cancer of the rectum there is commonly marked tenesmus. Blood, visible or occult, often appears in the stools and, after the occurrence of ulceration, pus, and rarely, shreds of the new growth itself may be present. When the tumor is situated in the lower bowel the stools are frequently of small diameter and of peculiar form—"stenosis feces." Cachexia and anemia are constant features of the later stages. In many cases roentgenography or proctoscopy yields evidence leading to an early diagnosis. Symptoms of acute obstruction may supervene at any time in consequence of fecal impaction, kinking of the bowel, intussusception, or simple intestinal paralysis.

*Cicatricial Stricture and Atresia.*—In the vast majority of cases cicatricial stricture of the bowel results from the healing of an ulcer. The most important ulcers in this respect are those due to syphilis, tuberculosis, peptic ulcers of the duodenum, stercoral and traumatic ulcers. Stricture following dysenteric ulceration is very uncommon and that following typhoid ulceration is exceedingly rare. The favorite sites of cicatricial stenosis of the bowel are in the rectum and colon. Rectal strictures are much more frequent in women than in men, and are usually the result of syphilis, tuberculosis, surgical operations, or trauma (including obstetric injuries). Intestinal strictures of tuberculous origin are usually single, but they may be multiple. When single they are localized, as a rule, near the ileo-cecal valve; when multiple they are almost invariably situated in the ileum. Two forms occur, the one being caused by cicatrization of the ordinary superficial ulcer; the other, the more common form, resulting from marked inflammatory thickening of the bowel-wall, the ulcer itself remaining intact (hyperplastic stricture).

Congenital atresia of the intestine, excluding imperforate rectum and anus, is very rare. Of 89 cases, 29 occurred in the duodenum, 54 in the jejuno-ileum, and 6 in the upper portion of the colon.[1] The symptoms of acquired stricture are those of gradually progressing enterostenosis. Energetic peristaltic waves visible through the abdominal wall are often an important feature. In cases of rectal stenosis the diagnosis, both as regards the existence of a stricture and the character of the cicatricial process, is, as a rule, readily made, but it is often difficult or impossible to determine at once whether a stenosis high in the bowel is due to a cicatrical stricture or to carcinoma. The differential diagnosis must rest upon a careful consideration of the history and all the facts of the case. The symptoms of congenital atresia of the bowel are acute and rapidly progressive.

*Dynamic Obstruction.*—Although this form of intestinal obstruction has a somewhat varied etiology (see p. 477), it is most commonly seen as a concomitant of peritonitis or following intra-abdominal operations (post-operative intestinal paralysis). There is good evidence to show that even postoperative intestinal paralysis is not always a purely reflex or functional condition, but is in some cases a manifestation of slight peritoneal infection. Prolonged operations and those requiring much handling of the abdominal viscera are the ones most likely to be followed by intestinal obstruction. The clinical picture of paralysis of the intestine is very similar to that of acute mechanical obstruction of the bowel. Fecal vomiting, however, is not so common in the former as in the latter. Difficulty is sometimes experienced in distinguishing between post-operative intestinal paralysis and frank peritonitis, but speaking generally, muscular rigidity, diffuse tenderness, fever and leucocytosis are in favor of peritonitis.

[1] Schlegel, quoted by Braun, Beiträg. z. klin. Chirurg., 1902.

**Diagnosis.**—This is concerned with the differentiation of intestinal obstruction from other conditions, with the site of the obstruction, and the character of the lesion producing the obstruction. The diagnosis of acute intestinal obstruction is in most cases comparatively easy. Difficulty may arise, however, if no exact history is obtainable, if opium has been used freely, or if peritonitis has already developed. The conditions that most often come into question are *acute peritonitis, acute appendicitis, perforation of the hollow viscera, acute pancreatitis and rupture of an ectopic pregnancy.* In all of these conditions the symptoms of onset may be similar to those of acute intestinal obstruction; indeed, in any one of them an actual dynamic or paralytic obstruction may supervene, so that the diagnosis of the primary lesion may be very uncertain. *Acute peritonitis*, in particular, is a frequent source of difficulty, as in many cases of acute obstruction this condition is present as a complication after the second or third day. Speaking generally, fever, leucocytosis, continuous pain, diffuse tenderness, rigidity of the abdominal wall are indications of peritonitis, and occurring at the onset are strongly opposed to intestinal obstruction as the primary condition. *Severe colic*, whether intestinal, biliary or renal, and *torsion of an ovarian cyst* or *of an undescended testicle* sometimes imitate acute obstruction of the bowel and may even produce the dynamic (reflex) form of the disease, but a careful consideration of the history and of the order in which the symptoms have appeared will usually lead to a correct diagnosis. *Acute dilatation of the stomach* may bear a striking resemblance to acute intestinal obstruction. In the former, however, retention of feces and gas is rarely complete, there is vomiting of large quantities of non-feculent material, and marked relief is afforded by the use of the stomach-tube and by postural change. In children the intestinal crises of *Henoch's purpura* may so exactly simulate obstruction of the bowel that no diagnosis is possible before the occurrence of arthritis or characteristic skin lesions—purpura, angioneurotic edema, or erythema. Intestinal paralysis from *thrombosis* or *embolism of the mesenteric vessels* may offer insurmountable obstacles to diagnosis. *Angina abdominis* occasionally proves confusing, but usually the paroxysmal character of the symptoms and the other indications of general arteriosclerosis give the clue. Even *hysteria* has been known to produce nearly all of the symptoms of acute intestinal obstruction, including the fecal vomiting (Sanders, Bregmann, Treves, Schwartz[1]).

A positive diagnosis of the exact site of the obstruction cannot always be made. In general a sudden onset with severe pain, early and frequently repeated vomiting, uniform distention of the central portion of the abdomen, marked oliguria, excessive indicanuria, and early and pronounced toxemia point to the small intestine as the site of the occlusion. A comparatively slow course, and limitation of the intestinal distention to the lateral and upper aspects of the abdomen suggest that the lesion is in the colon. Fecal vomiting is less frequently observed and usually occurs later in obstruction of the large bowel than in obstruction of the small one. So-called stenosis feces and tenesmus indicate that the rectum or the lower part of the large bowel is involved. In some instances the site of obstruction is disclosed by a rectal or vaginal examination, in others it is clearly shown by the presence of a tumor or of active peristalsis ceasing abruptly at a particular point. In chronic cases valuable assistance is often obtained from x-ray examinations.

It is not always possible to determine the exact nature of the lesion causing obstruction without resort to celiotomy, but a definite conclusion may often be reached if the age of the patient is considered, if the previous history of the case and the mode of onset are carefully reviewed, and if a thorough physical

[1] St. Petersburg med. Woch., 1904, xxix, No. 21.

examination is made, not neglecting the various hernial orifices, the rectum, or the vagina.

**Prognosis.**—The prognosis depends upon the nature of the obstruction and also to a great extent upon the promptness with which appropriate treatment is instituted. In acute obstruction from strangulation, invagination or volvulus spontaneous recovery is exceedingly rare, and, unless timely treatment affords relief, death almost invariably occurs within a few days. Obstruction due to foreign bodies, including gall-stones, not rarely undergoes spontaneous cure, and that due to fecal accumulation can usually be overcome by non-operative measures. Paralysis of the bowel following operations or resulting from peritonitis is a very grave condition; that following reflex irritation is much less serious. In chronic intestinal obstruction the symptoms often persist for months, or even years, and a permanent cure is rarely obtained except by operation. Deaver and Ross[1] report 276 cases of acute intestinal obstruction with a mortality of 42 per cent., Richardson,[2] 118 cases, with a mortality of 41.5 per cent., and Finney[3] 245 cases with a mortality of 36 per cent.

**Treatment.**—The treatment of intestinal obstruction is almost exclusively surgical. The mortality of cases submitted to operation is still very high, but this is mainly due to the reluctance of the internist to seek the advice of the surgeon or of the patient to accept surgical aid at an early stage. In invagination, if the patient is seen within the first twenty-four hours, a single attempt may be made to relieve the condition by a high rectal enema of lukewarm water. The patient's pelvis should be well raised and the fluid should be introduced by gravity through a long flexible tube from an elevation, in the case of a young child, of about 4 feet. The likelihood of relief from this procedure is small, and once it has been employed without success operation should be no longer delayed. In case a foreign body has been swallowed and the symptoms are not in the least urgent, the plan of feeding the patient with large quantities of mashed potatoes and other soft foods, as recommended by Billroth, should be adopted. Large doses of atropin—$\frac{1}{60}$–$\frac{1}{40}$ gr.—0.001–0.0016 gm.—may also be given, as this drug tends to allay intestinal spasm, which is sometimes responsible for the obstruction. With these exceptions, operation should be undertaken at the earliest moment possible in every case in which the symptoms are those of acute mechanical obstruction of the bowel, even if the exact nature of the obstruction is not apparent. All food and fluid by the mouth should be withheld, and under no circumstances whatever should a purgative be administered. Morphin should be avoided, if possible, at least until the diagnosis of obstruction has been made and preparations for operation are under way. If used early it is likely to produce an apparent improvement, and in so doing, to conceal the gravity of the patient's condition. Gastric lavage, frequently repeated if the patient is not too much exhausted, is a valuable measure, especially when the vomiting is persistent. The removal of the stomach contents tends not only to lessen vomiting, but also to reduce the pressure in the bowel and thus indirectly to relieve the pain. Enemas of saline solution, 3 or 4 quarts, in the first 24 hours, as recommended by Murphy, are also of much service in aiding elimination and in combating dehydration and toxemia. If the constitutional symptoms are severe, subcutaneous or intravenous injections of saline solution may be substituted for the enteroclysis.

Paralysis of the bowel from causes other than peritonitis not rarely yields

[1] Annals of Surgery, 1915, lxi.
[2] Boston Med. and Surg. Jour., 1920, clxxxiii, No. 10.
[3] Surg., Gyn. and Obstet., 1921, xxxii, No. 5.

to medical treatment. Hot applications, in the form of turpentine stupes, or if these fail, cold applications, may prove beneficial. Colonic douches of saline solution or enemas containing stimulating drugs, such as asafetida or oil of turpentine, are often useful. Good results may also follow the subcutaneous administration of pituitary extract (1 mil) or of physostigmin sulphate—1/60 to 1/40 gr. (0.001–0.0016 gm.) every four hours.

Obstruction of the bowel due to fecal impaction may usually be overcome by copious enemas of warm soapy water, frequently repeated, the rectum first being emptied, if necessary, with the finger or some blunt instrument. If the mass is very hard an injection of cotton-seed oil (6–8 oz.—180–235 mils) or of dried ox-gall (℥ii—8.0 gm.) in water (Oj–0.5 L.) may first be used to soften it. Gentle abdominal manipulation is sometimes helpful in effecting the removal of collections in the colon. Cathartics must be employed with caution and only after the rectum has been emptied. The most useful are the salines, castor oil, and liquid petrolatum.

In chronic obstruction of the bowel, the result of tumor or stricture, medical treatment is only palliative and consists chiefly in careful regulation of the diet and the use of mild laxatives and enemas. If temporary occlusion with violent peristaltic movements supervenes, atropin, and not purgatives, should be given. Warm applications are useful.

## TUMORS OF THE INTESTINES

**Carcinoma.**—Carcinoma is the most common tumor of the intestines. Sarcoma is rare, and so are adenoma, lipoma and other benign growths. Between 5 and 10 per cent. of all carcinomas are in some portion of the intestines. The parts most frequently affected are the rectum, sigmoid flexure and cecum. Only about 3 per cent. of intestinal carcinomas are in the small bowel. The majority of cases occur in persons more than 40 years of age, but it is noteworthy that the proportion of cases occurring between the ages of 20 and 40 is considerably larger than usually obtains in carcinoma elsewhere. The new growth generally appears as a narrow indurated ring of tissue, causing a stricture of the bowel (annular scirrhus), although occasionally, especially in young persons, it takes the form of a well-defined fungous mass. Metastasis to other organs rarely occurs until late in the disease.

In the majority of cases there are symptoms of gradually developing intestinal stenosis, with a palpable tumor, and later, as the growth advances, loss of weight, anemia, and cachexia. Stenosis of the bowel is indicated by increasing constipation or alternating constipation and diarrhea, recurring attacks of colicky pain and abdominal distention, and visible peristaltic movements. Occult blood usually appears in the stools, and in many cases visible blood, mucus and pus are also present, especially when the lower part of the large bowel is affected. The tumor is firm, usually tender, and, unless adhesions have already formed, freely movable. A gurgling of gas through the tumor may sometimes be heard. If the growth is situated in the rectum or sigmoid flexure its presence may be revealed only by digital palpation through the anus or by the use of the enteroscope. In other cases x-ray examinations afford valuable aid in diagnosis. Malnutrition and anemia do not appear, as a rule, until the disease is far advanced, and unless the growth is near the anal margin the inguinal lymph-nodes are rarely enlarged. In

carcinoma of the colon or of the small intestine pain is usually absent, except during the attacks of colic. In carcinoma of the rectum, however, pain in the region of the sacrum, or in the distribution of the sciatic nerve, rectal tenesmus, and vesical irritability are sometimes prominent symptoms.

Many variations in the clinical picture of carcinoma of the bowel are observed. In some cases the earliest manifestation is the occurrence of intermittent intestinal obstruction; in others, the primary condition is overshadowed by the sudden development of diffuse (perforative) peritonitis or of a circumscribed abscess in the cecal region, suggesting appendicitis; and occasionally the disease remains latent until peritoneal carcinosis with ascites has developed, until metastases have formed in the liver, brain, or some other organ, or until the growth has involved the bladder or kidney, producing symptoms of cystitis or of renal infection.

In carcinoma of the duodenum symptoms and signs of pyloric obstruction with dilatation of the stomach are usually present. If the second portion of the duodenum is involved (ampullary carcinoma) there is in addition progressive jaundice; if the third portion is affected (infra-ampullary carcinoma) there may be no jaundice, but the vomitus is often rich in bile and pancreatic juice and the stools are likely to be clay-colored. About 65 per cent. of all duodenal carcinomas are situated beyond the ulcer area, at the ampulla.

The *diagnosis* of carcinoma of the bowel at an early stage is often attended with difficulty, but undoubtedly many grievous errors would be avoided if careful examinations, not only of the abdomen, but also of the rectum, were more frequently made in cases of chronic digestive disturbance, and if it were more generally recognized that the appearance of blood and mucus in the evacuations or of symptoms of intestinal stricture, usually denotes malignant disease. Mucous colitis, pericolitis with kinking of the bowel, diverticular obstruction, and fecal impaction sometimes cause confusion. Tumors about the cecum, the result of appendicitis, tuberculosis, or actinomycosis, may closely simulate carcinoma. At the hepatic flexure it is necessary to exclude tumors of the liver, kidney and gall-bladder, and in the rectum, hemorrhoids, syphilis, tuberculosis, and amebic dysentery. The differentiation of duodenal carcinoma from carcinoma of the pylorus or common bile-duct is extremely difficult and usually impossible.

*Treatment.*—Operative measures offer the only possibility of cure. In the hands of an experienced surgeon and with a judicious selection of cases the mortality of resection of the colon should not exceed 20 per cent. and of that of the rectum 15 per cent. Mayo[1] found that of the patients who had recovered from colectomy and who had been operated on more than 5 years before the date of the study 54 per cent. were still alive. Mayo[2] also found that of the patients who survived resection of the rectum or rectosigmoid, at least 33.3 per cent. lived 3 years or more, and 28.3 per cent. lived five years or more after operation. Kuttner's figures,[3] based on a series of 600 cases, are similar.

**Sarcoma.**—Compared with carcinoma, sarcoma of the bowel is very rare. No age is exempt, but the large majority of cases are in persons less than 40 years of age. The round-cell type is the most frequent, although all types have been observed. The small bowel and the rectum are the portions of the intestines most often affected. In the large bowel the cecum is the favorite site. In contrast with carcinoma, deterioration of the general health occurs early and is out of all proportion to the local disturbance. A

[1] Jour. Amer. Med. Assoc., 1916, lxvii, 18.
[2] Annals of Surgery, 1916, lxiv, No. 3.
[3] Münch. med. Woch., 1921, lxvii, No. 28.

tumor is usually present, and may reach a large size, but symptoms of obstruction are uncommon, and when they do occur are usually the result of secondary invagination or volvulus. The abdominal lymph-nodes are frequently involved by metastasis and secondary growths not rarely occur in other organs. Surgical treatment if undertaken sufficiently early offers a fair chance of recovery. In cases not subjected to operation the average duration of life from the onset of symptoms is about six months.

**Multiple Adenomatous Polyposis of the Intestines** is a rare condition. Doering[1] collected 52 cases and Soper[2] in 1916 collected 8 additional ones and reported one of his own. Children are more frequently affected than adults and males more frequently than females. The favorite sites are the rectum, the sigmoid, and the splenic and hepatic flexures of the colon. The small intestines are rarely involved. The usual symptoms are vague abdominal pain, rectal tenesmus and diarrhea, with the passage of mucus and blood in the stools. In some instances enterorrhagia is for a time the only indication. Proctoscopy and roentgenography may aid in the diagnosis. In a few cases partial or complete resection of the colon has been successfully performed.

**Carcinoma of the Vermiform Appendix.**—Statistics show that about 0.5 per cent. of all appendicular lesions are carcinomatous. The disease is apparently somewhat more common in females than in males, and is peculiar in developing comparatively early in life, the average age being about 30 years. The symptoms are those of acute or chronic appendicitis, and, therefore, a clinical diagnosis is virtually impossible. It is noteworthy that the condition is almost always benign, although metastasis or extension has been observed in a few instances.

## EMBOLISM AND THROMBOSIS OF THE MESENTERIC VESSELS

Occlusion of the mesenteric vessels is comparatively uncommon. The large majority of the subjects are more than 30 years of age, and males are much more often affected than females. In 366 cases collected by Trotter,[3] the arteries were involved in 53 per cent., the veins in 41 per cent., and both in 6 per cent. The superior mesenteric vessels are obstructed much more frequently than the inferior.

The most common cause of arterial occlusion is embolism originating from acute or chronic endocarditic changes, or less frequently from thrombi in the aorta or heart. Occlusion of the mesenteric vein is due to thrombosis, the result of stasis in the portal circulation (cirrhosis of the liver, pylephlebitis, etc.), or less frequently of a septic process in the appendix or pelvis. Occlusion of the mesenteric vessels is usually followed by hemorrhagic infarction and necrosis of a segment of the intestine, and, if the patient survives sufficiently long, by peritonitis. The most constant clinical manifestations are sudden intense pain in the abdomen, vomiting, sometimes bloody, diarrhea with profuse bleeding from the bowel, general tympanites, and severe shock. In some instances there is constipation instead of diarrhea, and occasionally the clinical picture is simply that of acute intestinal obstruction of the paralytic type. Acute peritonitis not uncommonly supervenes. Rarely a tumor (mesenteric hematoma) has been felt in the region of the infarction. In

[1] Arch. f. klin. Chir., 1907, lxxxiii, S. 194.
[2] Amer. Jour. Med. Sci., 1916, cli, No. 3.
[3] Trotter: Embolism and Thrombosis of the Mesenteric Vessels, Cambridge, 1913.

a small group of cases, chiefly of venous thrombosis, the onset is insiduous and the symptoms are more or less vague and remittent. The diagnosis is rarely made with certainty. The condition may be suspected when the aforesaid symptoms ensue in the course of endocarditis or aortitis, and especially if emboli coincidently occur elsewhere or a tumor suddenly appears in the abdomen. Among the conditions that must be differentiated are rupture of the hollow viscera, acute intestinal obstruction, acute pancreatitis, and ruptured ectopic pregnancy. The prognosis is extremely grave. Unless operation with resection of the affected segment of bowel is undertaken at an early stage, the acute cases nearly always end fatally within a few days. Spontaneous recovery is possible, however, if the obstruction occurs so slowly that a collateral circulation can develop. Occasionally septic embolism of the mesenteric arteries, the result of ulcerative endocarditis, gives rise to aneurysm. Nine of the 16 cases of mesenteric aneurysm collected by Gallavardin[1] had this origin. Estimates of recoveries under operative treatment range from 12 to 36 per cent. The lowest of the percentages is probably the most accurate.

## ENTERORRHAGIA

**Etiology.**—Loss of blood by the way of the intestine does not always indicate enterorrhagia. Somewhat frequently the source of the bleeding is in the stomach, the throat, or the nose, or even in the lungs, some of the blood that enters the mouth in hemoptysis not rarely being swallowed and eventually entering the intestine. Occasionally, also, blood appears in the feces as a result of the rupture of an aneurysm of the abdominal aorta into the bowel, of acute hemorrhagic pancreatitis, or of a lesion involving the blood-vessels of the liver, such as aneurysm of the hepatic artery or abscess.

True intestinal hemorrhage may be due to a great variety of causes, but of these the most common are (1) various forms of intestinal ulceration—peptic, carcinomatous, typhoidal, amebic, tuberculous, syphilitic, and simple; (2) acute inflammation of the intestine, caused by infection or irritant poisons; (3) general venous hyperemia of the intestine due to diseases of the heart or, much more frequently, to cirrhosis of the liver or primary splenomegaly (splenic anemia); (4) trauma, the injury of the bowel being sustained from without or produced directly by a foreign body or hardened feces; (5) intussusception and, in exceptional cases, volvulus of the intestine; (6) certain constitutional diseases or intoxications with a hemorrhagic tendency, such as pernicious anemia, leukemia, scurvy, purpura, septicemia, yellow fever, severe icterus, and phosphorus poisoning; (7) hemorrhoids and anal fissure and fistula. Exceptional causes of enterorrhagia are (8) embolism and thrombosis of the mesenteric vessels, (9) helminthic infection of the intestine —ankylostomiasis, schistosomiasis (bilharziasis), etc., (10) multiple polyposis of the intestinal tract, (11) changes in the intestinal arteries and capillaries, such as occur in amyloid disease and nephritis, and (12) primary venous varicosites of the small intestine.

Intestinal hemorrhage in the new born (melena neonatorum) has a varied etiology. Among the more important causes may be mentioned prolonged asphyxia with intense venous stasis of the bowel, congenital syphilis, septic infection, ulceration of the intestine, hemophilia, and the rare and obscure condition commonly known as Buhl's disease.

[1] Gaz. Hebd. de Méd. et de Chir., 1901, No. 82.

**Symptoms.**—The degree of hemorrhage varies greatly. In many instances the blood is passed in such small quantities that it does not change the color of the stools and is recognizable only by microscopic examination or chemical tests (occult blood). On the other hand, the bleeding may be so profuse that death rapidly ensues. Between these two extremes every gradation of enterorrhagia is observed. The quantity of blood in the stools does not always indicate the degree of hemorrhage, for not rarely a large proportion of the blood is retained in the bowel and occasionally death occurs before any issues from the body. The most common causes of profuse intestinal bleeding are typhoid fever, peptic ulcer and cirrhosis of the liver.

The appearance of visible blood in the stools depends on the severity of the hemorrhage and the time the blood has remained in the intestine. Blood coming from the upper part of the small bowel or the stomach, unless the quantity is very large, is usually evacuated as black tar-like fluid or masses (melena); while blood coming from the lower part of the small intestine, the colon or the rectum, especially if passed quickly, and the loss is considerable, is as a rule, so little altered that it is readily recognized as blood. In hemorrhage into the upper portion of the duodenum a portion of the blood or, exceptionally, the whole of it may leave the body by way of the stomach.

The constitutional effects, results and treatment of enterorrhagia are in general similar to those of hematemesis (see p. 448).

## SPLANCHNOPTOSIS

### (Glénard's Disease)

**Definition.**—As applied to the viscera, the term ptosis signifies a sagging or gravitational displacement of an organ, due to congenital or acquired weakness in its normal support. Any or all of the abdominal viscera may be affected. Falling of the stomach is known as *gastroptosis;* of the intestines, as *enteroptosis* (*coloptosis*); of the kidney, as *nephroptosis;* of the liver, as *hepatoptosis*, and of the spleen, as *splenoptosis*. More than one organ is involved in the large majority of cases, and therefore the term *splanchnoptosis* is, as a rule, properly applicable to the condition. Although previously recognized, visceral ptosis did not attract much attention until 1885, when Glénard[1] published a report associating it with nervous dyspepsia and ascribing it to relaxation of the hepatocolic ligament, the result of inherent weakness.

**Etiology.**—The causes of splanchnoptosis are obscure, although it is probable, as Glénard assumed, that a constitutional defect is usually the basic condition and that persons with a congenital delicacy of tissue or with certain anomalies of body formation are especially predisposed to the disease and are more easily affected by exciting causes which have little or no effect on others. Stiller, who is a firm believer in the congenital origin of visceral ptosis, lays stress on the so-called *habitus enteropticus*, which is characterized by a long, narrow thorax, with an acute subcostal angle and also, in some instances, an abnormally movable (floating) tenth rib. The abdomen is relatively short and often unduly prominent. The abdominal muscles may be well developed and firm, but, as a rule, they are flabby and relaxed, and not rarely slight separation of the recti is also observed. In the case of nephroptosis, Wolkow and Delitzin[2] attach much importance to abnormal

[1] La Semaine Médicale, 1885.
[2] Die Wanderniere, Berlin, 1899.

shallowness of the paravertebral fossæ. Among the factors capable of acting as exciting causes of splanchnoptosis may be mentioned the pressure of clothing (tight lacing, heavy skirts), various diseases associated with rapid loss of fat, and, especially, weakening of the abdominal muscles by frequent pregnancies, recurrent ascites, etc. Direct or indirect violence appears to play a part in some instances; it is probable, however, that traumatism is more potent in exciting symptoms in an organ that is already displaced than it is in causing the displacement itself. Women are much more subject to the disease than men.

**Symptoms.**—In many cases visceral ptosis gives rise to no symptoms, physical examination alone revealing its presence. In other cases the general phenomena of neurasthenia—fatigue after moderate exertion, emotional depression, headache and backache, palpitation of the heart, and coldness of the extremities—are more or less conspicuous, and to these are often added a number of abdominal symptoms common to many conditions, such as dragging pain, epigastric throbbing, nausea, flatulence and constipation. In a third group of cases local disturbances, chiefly of a mechanical nature and often referable to the organ mainly at fault, are especially prominent. Thus, as a result of the general myasthenia or as a consequence of duodenal kinking caused by the ptosis itself there may be definite indications of gastric atony or even of gastrectasis; owing to twisting of the ureter there may be aching in the back or flank, with frequent urination or intermittent polyuria, or, less frequently, so-called Dietl's crises, which consist of attacks of severe pain with nausea and vomiting, cold sweats, oliguria, and hematuria, and which are very suggestive of renal colic; as a result of traction on the colon there may be obstinate constipation and the multiple symptoms supposed to be due to the absorption of the products of intestinal fermentation; finally, owing to kinking of the bile-duct there may be slight jaundice, accompanied, perhaps, by paroxysms of pain simulating biliary colic. Whatever the symptoms, they are usually decreased by the prone position and increased by standing and walking. The relation of the nervous phenomena to splanchnoptosis has been much discussed. Probably in the majority of cases the same causes that favor the development of neurasthenia also favor the occurrence of visceral ptosis, and when the two conditions coexist they react on each other deleteriously (Steele). It is conceivable, however, that in some instances local disturbances directly dependent on visceral ptosis may be an important factor in initiating nervous symptoms. Doubtless, the pseudo-hypochrondriasis occasionally observed with nephroptosis is sometimes the result of worry occasioned by a knowledge of the fact that an anomaly exists. For this reason patients' attention should not be drawn to movable kidney unless there is good reason for believing that it is the cause of their symptoms.

The *objective signs* of splanchnoptosis are often more definite than the symptoms. However, there is no concensus of opinion among internists as to what actually constitutes gastroptosis. Certainly descent of the greater curvature below the level of the umbilicus, when the subject is in the erect position, can no longer be regarded as an indication, as this position is not infrequently observed in persons who are apparently normal. Perhaps, one may concede the existence of gastroptosis if in the absence of gastrectasis the lower pole of the stomach is well below the navel level when the patient is in the recumbent position. The shape and position of the stomach are best determined by the x-ray after the administration of an opaque meal. Formerly, the organ was outlined by percussion after it had been artificially inflated, but this method of examination is likely to yield misleading results, and therefore it has been largely abandoned.

In many cases of prolapse of the stomach there is also ptosis of the colon, the transverse portion of which often occupies a position below the lower gastric pole and occasionally lies immediately above the pubic symphysis. A deficiency in the gastrocolic omentum is probably an important factor in causing downward displacement of the transverse colon and weakness of the attachment fixing the ascending colon to the posterior abdominal wall seems to be chiefly responsible for prolapse of this portion of the large intestine. Owing to its strong attachment at the splenic flexure, the descending colon is not often involved. When the attachment of the lower part of the ascending colon is weak there is a tendency for the cecum to dilate and to sag toward the true pelvis, thus producing the condition which Wilms[1] has termed the "cecum mobile" and which he believes is frequently confused with chronic appendicitis. These anomalies in the position of the colon are well shown by the roentgen-ray.

Normally, the kidneys possess a slight range of motion and when the abdominal walls are thin and relaxed the lower pole of the right one is sometimes palpable. When the entire kidney or a large part of it can be felt during deep inspiration the condition is known as *movable kidney*, and when the whole organ is readily palpable and can be freely moved about in the abdominal cavity the condition is termed *floating kidney*. In some instances the displaced organ is retained in an abnormal position by adhesions. The right kidney, probably owing to its relation to the liver and to the drag of the ascending colon with its great weight of feces, is much more frequently affected than the left, or in the proportion of about 8 to 1. Occasionally both organs are involved.

The presence of nephroptosis is best determined by bimanual palpation. The patient lies on his back with the thighs slightly flexed. The examiner's left hand is pressed against the lumbar region so as to push the kidney forward, while his right hand is firmly applied to the abdominal wall. The patient is then directed to take a deep breath, when the kidney, if loose, will be felt as a smooth, round body with more or less mobility. Sometimes the examination is better performed while the patient is in the knee-elbow position or is standing and bending slightly forward with the hands resting on a table. In floating kidney the whole organ is readily palpable and may be recognized by its size, shape, consistence and slippery feel, by the possibility of replacement, and very rarely by the pulsation of the renal artery.

Hepatoptosis and splenoptosis are much less common than nephroptosis, and may easily be recognized, as a rule, by palpation and percussion.

**Diagnosis.**—The diagnosis of splanchnoptosis is not often difficult. In some cases the history of persistent neurasthenia and of vague digestive disturbances together with the general appearance of the patient—emaciation, sallow complexion, long narrow thorax, epigastric pulsation, flabby abdominal walls, and pendulous abdomen—almost at once proclaims the condition. In many cases, however, diagnosis can be reached only by careful physical examination, including a roentgenographic study. Among the conditions which may be mistaken for floating kidney are fecal tumor, distended gall-bladder, pedunculated myoma of the uterus, and tumor of the ovary, omentum, or colon. The ectopic or congenitally misplaced kidney differs from a movable kidney which has wandered from its normal position in having, as a rule, a short pedicle and an anomalous blood supply. It is usually fixed in the pelvis at a level with the promontory of the sacrum (Judd and Harrington[2]).

[1] Deutsch. med. Woch., 1908, ii, 1756.
[2] Collected Papers of the Mayo Clinic, 1918, x, 257.

**Complications.**—Gastroptosis does not necessarily impair in any way the digestive functions, but occasionally by kinking the pylorus it retards the discharge of food from the stomach and so brings about a certain degree of gastrectasis. Enteroptosis may lead to intestinal stasis with possibly resultant auto-intoxication. Occasionally, splanchnoptosis by dragging on the mesentery causes obstruction of the terminal portion of the duodenum with dilatation of the cephalad portion—a condition usually characterized by abdominal pain, recurrent vomiting, and obstinate constipation, and likely to be mistaken for chronic cholecystitis or chronic appendicitis. A movable kidney is more susceptible to infection than one that is fixed, and, according to Howard Kelly, in 1 of every 7 cases of nephroptosis that give symptoms there is a beginning hydronephrosis. Twisting of the pedicle of a wandering spleen may result in thrombosis of the splenic vein with localized peritonitis, or, as in a case reported by Osler, in acute necrosis of the organ.

**Prognosis.**—However much it may disturb the health of the patient, splanchnoptosis rarely endangers life. In many cases, too, we may hope for marked alleviation, even without recourse to surgical measures. Complete relief from symptoms, however, does not necessarily imply anatomic cure.

**Treatment.**—The chief indications are to elevate the prolapsed organs and to keep them in place by providing adequate support, to relieve any local disturbances that may occur in the affected organs, to correct any existing postural abnormalities and to improve the general nutrition. To keep the prolapsed organ in its normal position mechanical supports which make pressure from below upward and backward are often of value. The support may consist (1) of strips of adhesive (zinc oxid) plaster, about 3 inches wide, passed obliquely around the abdomen from the region of the symphysis upward and backward, crossing in front and back; (2) of a specially designed abdominal binder; or (3) of the so-called straight-front corset. It is important that the binder or corset should be applied while the patient is in the supine posture with the thighs flexed, and removed only when he is again recumbent. Neither binder nor corset is likely to be of service if the abdomen is scaphoid or the ptosis is extreme. In nephroptosis it may be necessary to use a suitable pad in addition to the other means of support. Rest in the horizontal position, particularly after each meal, often affords much relief. In order to correct postural abnormalities and to improve the tone of the abdominal muscles special gymnastic exercises are unquestionably of much benefit. Constriction of the lower portion of the thorax by tight clothing of any kind must be forbidden. Improvement in the general nutrition is best secured by dietetic and hygienic measures. Liberal feeding is usually required, but in all cases the diet should be carefully adapted to the digestive capacity of the patient. Hydrotherapy is often very useful. Tonics, especially strychnin, are sometimes indicated. Neurasthenia will require the general measures advocated in the section dealing with that condition. The treatment of constipation and other local disturbances is the same as for like conditions in normally placed organs.

*Surgical Treatment.*—In carefully selected cases appropriate surgical treatment—suturing the prolapsed organ to an adjacent structure, shortening of its supporting ligaments, etc.—may afford complete relief, but frequently the results are more or less unsatisfactory. Relapse is common and not rarely the operation is followed by the formation of troublesome adhesions. Certainly, surgical treatment should not be recommended unless there are definite local disturbances which cause persistent discomfort or serious impairment of nutrition and which resist all other measures. Operation

undertaken for the relief of neurasthenic symptoms or vague disturbances referable to a number of organs is much more likely to do harm than good.

# DISEASES OF THE LIVER

## JAUNDICE OR ICTERUS

**Definition.**—The term jaundice is applied to a staining of the tissues and fluids of the body with bile pigment.

**Types.**—Until recent years it was held that jaundice never occurs without the participation of the liver, but is always the result of the resorption of bile pigment that has been formed and excreted by the hepatic cells. Indeed, Naunyn[1] still inclines to the view that in all cases of supposed extrahepatic jaundice there exists some minute obstruction of the biliary passages. The studies of Lyon-Caem, in France and of Whipple and Hooper, in America, however, seem to have proved conclusively that true bile pigment may occur in the urine after injections of laked blood, even with the liver excluded from the circulation. Exactly where the transformation of hemoglobin into bilirubin is effected under these circumstances is not known. As regards the bile salts, there is no evidence of any origin other than hepatic. While the subject of the genesis of bile pigment must still be considered as being in the controversial stage, it is nevertheless customary to speak of two types of jaundice; *Hepatogenous* or *obstructive* and *hematogenous* or *non-obstructive*.

*Obstructive jaundice*, the more common form of biliary pigmentation, may be caused by conditions originating in the walls of the bile-ducts or operating within the ducts or from outside. It may result from:

1. Inflammatory swelling of the ducts (cholangitis) or of the duodenal mucous membrane around the orifice of the common duct.
2. Stricture of the larger ducts, congenital or acquired.
3. Morbid growths of the ducts or foreign bodies in the ducts, such as gall-stones and parasites (roundworms, flukes, etc.).
4. Compression of the ducts by tumors or cysts of the liver or of the adjacent viscera.
5. Compression of the ducts by (*a*) enlarged lymph-nodes (carcinomatous, simple inflammatory, syphilitic or tuberculous); (*b*) peritoneal adhesions, due to peptic ulcer, gall-stones, etc.; (*c*) fibroid induration of the head of the pancreas (chronic pancreatitis); (*d*) aneurysm of the aorta, hepatic artery, or superior mesenteric artery; (*e*) fecal accumulations.
6. Kinking or torsion of the ducts, the consequence of hepatosis, nephroptosis, abdominal tumors, etc.
7. Spasm of the ducts. This has been suggested as the cause of the jaundice that very rarely occurs after intense emotional excitement, but it is possible that disturbance of the circulation within the liver is the important factor.

According to C. H. Mayo,[2] of all cases of jaundice, about 50 per cent. are due to cholelithiasis, 20 per cent. are due to catarrhal cholangitis, and 15 per cent. are due to carcinoma of the liver, pancreas, or biliary tract.

*True hematogenous jaundice* is observed in:

1. Chronic hemolytic icterus, congenital or acquired.
2. Some cases of pernicious anemia.
3. Certain cases of paroxysmal hemoglobinuria.

[1] Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1919, 31, 537.
[2] Surg., Gynec. and Obstet., 1920, xxx, 545.

The jaundice occurring in various bacterial or protozoal infections, such as acute infectious jaundice, syphilis and malaria, and in consequence of certain intoxications, such as may be caused by phosphorus, arsenic, trinitrotoluol, arseniuretted hydrogen, etc. may also be due to excessive destruction of the red blood-cells, but in most of these conditions hepatic damage sufficient to cause obstruction of the smaller bile-ducts is also present. The changes in the liver responsible for the retarded biliary flow and the reabsorption of the bile into the general circulation may be a radicular cholangitis excited by the excretion of the poisons through the liver, compression of the biliary capillaries by swollen hepatic cells, or disorganization of the biliary capillaries, with the escape of bile into the lymph-spaces. It is also possible, as Stadelmann[1] suggested, that the large amount of hemoglobin brought to the liver may result in the excessive excretion of thick, viscid bile (polycholia) with plugging of the minute ducts.

**Effects of Bile-Pigments and Bile Salts.**—Having entered the general circulation the bile yields its pigment to the various tissues and to several of the secretions, especially the urine and sweat. Serous transudates and inflammatory exudates are almost constantly colored, but the tears, saliva, mucus secretions and milk, unless mixed with inflammatory exudates, are, as a rule, unaffected. The staining of the tissues is not uniform. The liver, kidneys, spleen, bloodvessel walls, skin and mucous membranes are especially involved, but the brain and nervous tissues, lungs (except in pneumonia), and cartilages are relatively unaffected. Clinically, the condition is first noticed in the conjunctiva and mucous membrane of the palate, although bile pigment appears in the urine twenty-four or forty-eight hours before these parts show the icteric tint. With the removal of the biliary obstruction the pigment is slowly discharged from the tissues, several weeks sometimes elapsing before the skin is entirely free.

The bile-pigments seem to be relatively non-toxic, although there is some evidence to the contrary. The bile-salts are believed to be toxic, slowing the pulse by stimulating the cardio-inhibitory center, causing cytolysis, retarding the coagulation of the blood, and depressing the central nervous system, inducing stupor and coma. The minor functional disturbances ordinarily observed in obstructive jaundice are apparently due in part to the toxic action of the bile itself and in part to the absence of bile from the intestinal tract. The profound intoxication that sometimes occurs in advanced hepatic disease with jaundice ("cholemia") is probably due not so much to reabsorbed bile as to infection of the biliary tract, preceding or following the stagnation of bile, to poisons which normally are rendered harmless by the liver, and to other poisons arising from interference with the metabolic functions of the liver.

The pronounced hemorrhagic tendency that occurs in persistent icterus may be due to the solvent action of the bile salts on the capillary endothelium or to interference with coagulation by the bile salts and bile pigments, the latter combining with the calcium of the blood and thus rendering it unavailable for the formation of fibrin. The conditions occurring in long-continued hepatogenous jaundice favor the formation of a so-called "vicious circle," for the reabsorbed bile salts by increasing hemolysis cause polycholia, which in turn intensifies biliary stagnation.

**Dissociated Jaundice.**—This term is applied to the occurrence of either bile salts or bile pigment separately in the blood or in the urine. Hoover and Blankenhorn[2] have shown that under certain conditions, not well under-

[1] Der Icterus u. seine verschied. Formen, Stuttgart, 1891.
[2] Arch. Int. Med., 1916, 18, 289.

stood, the plasma of the blood may retain a large amount of bile pigment and bile salts and yield none of either to the kidneys or to the tissues, that the liver may shunt either the pigment or salts into the blood stream independently (hepatic dissociation) and that in complete jaundice the kidneys may excrete only the bile salts, leaving the pigment in the blood (renal dissociation). Excepting in jaundice of hemolytic origin and in complete jaundice which has undergone renal dissociation bile pigment is not found without bile salts in the plasma. Bile salts without bile pigment in the plasma indicate genuine dissociated jaundice of hepatic origin.

**Symptoms.** *The Conjunctivæ and Skin.*—Jaundice appears first in the conjunctivæ, then in the skin of the entire body. The yellowish discoloration of the conjunctivæ due to masses of fat beneath the mucous membrane is not likely to be mistaken for jaundice as it occurs in patches and is unevenly distributed. The color of the skin varies according to the intensity and duration of the pigmentation from a pale yellow to an olive green. In long-standing cases it may be greenish-black, owing to oxidation of the bilirubin. Pruritus, or itching without eruption, is often a distressing symptom, especially at night, but it may be absent even when jaundice is pronounced. Upon which of the biliary constituents it depends is not definitely known. Occasionally the itching precedes the cutaneous pigmentation by days or weeks[1] and in this case it sometimes ceases with the appearance of the latter.

Actual lesions of the skin are rarely observed, but in chronic cases urticaria, spider angiomata, or xanthomata may develop. The last appear as soft yellowish plaques or nodules, usually multiple and symmetrically distributed, and with a predilection for the eyelids and the creases or folds of the joints.[2]

Discolorations of the skin resembling jaundice, such as may occur in chlorosis, pernicious anemia, malignant disease, hemochromatosis, Addison's disease, and carotinemia[3] may readily be excluded by the absence of bile pigment from the conjunctivæ and urine.

*The Urine.*—The color of the urine varies from brownish-yellow (beer-brown) to brown or brownish-green. The foam that forms when it is shaken is persistently yellow. Similar discolorations of the urine due to blood-pigment, santonin, rhubarb, etc., may be excluded by Gmelin's test.[4] Traces of albumin are often present after a time in persistent jaundice, and even in the absence of albuminuria, hyaline tube-casts are almost always found. Urobilinuria is slight or absent when there is complete obstruction of the common bile-duct, but it is pronounced in hemolytic icterus with a normal liver. As a result of the increased intestinal putrefaction in obstructive jaundice, the indican and ethereal sulphates of the urine are in excess.

*Digestive Tract.*—Impairment of appetite, a bitter taste in the mouth, flatulency and a tendency to constipation are frequent causes of complaint. In hepatogenous jaundice the stools are, as a rule, clay-colored, or if the biliary obstruction is complete, grayish-white, the pale color being due partly to an absence of the bile-pigments, and partly to an excess of fat, the cleavage and absorption of which are interfered with by the lack of bile.

[1] For literature, see Riesman, American Medicine, Feb., 1907.

[2] See Futcher, Amer. Jour. Med. Sci., Dec., 1905.

[3] Yellowish pigmentation of the body from the liberal use of vegetables, especially carrots, rich in the lipochrome, carotin. See Hess and Myers (Jour. Amer. Med. Assoc., Dec. 6, 1919), Kaupe (Münch. med. Woch., Mar. 21, 1919), Stoelzner (Münch. med. Woch., April 11, 1919), Klose (Münch. med. Woch., April 11, 1919).

[4] If fuming nitric acid be overlaid with icteric urine a ring of green, blue and red forms at the point of contact.

As a result of the intestinal indigestion, rather than from the loss of the supposed antiseptic action of the bile, intestinal putrefaction may become more active and the stools more fetid.

The liver is often enlarged and tender in obstructive jaundice owing to the stasis of bile. The gall-bladder is also distended in many cases, but in jaundice due to the impaction of a gall-stone in the common duct it is usually small, in consequence of previous calculous irritation (Courvoisier's law).

*Circulatory System.*—In the early stages of jaundice, especially of the catarrhal form, the heart's action may become somewhat slow and irregular, and the blood-pressure may fall. These symptoms are believed to be due to stimulation of the cardio-inhibitory center by the bile salts.

In moderate degrees of jaundice of short duration the blood shows virtually no changes other than discoloration of the plasma. As previously pointed out bilirubin and bile salts may both be present in considerable quantity in the plasma without the sclera or skin showing any discoloration. Long-continued obstructive jaundice results in more or less anemia and a pronounced lengthening of the coagulation time of the blood. Hemorrhages into the skin and from the mucous membranes are not uncommon, and in severe cases surgical operation may be followed by dangerous or even fatal bleeding. Jaundice, *per se*, apparently does not cause leucocytosis. As was pointed out by Grünbaum,[1] the blood of jaundiced patients may give the Widal reaction with a typhoid culture.

*Nervous Symptoms.*—Headache and mental depression are common symptoms, even in mild forms of jaundice, and are probably due to the accompanying gastro-intestinal disturbances. Derangements of sight, such as yellow vision (xanthopsia) and night-blindness (nyctalopia), are exceptionally noted. In chronic cases delirium, stupor and coma ("cholemia") occasionally supervene and lead to death in a few days.

The symptoms of true hematogenous jaundice are much the same as those occurring in jaundice of obstructive origin, but the staining of the skin is, as a rule, less pronounced, the stools remain cholic, bile-salts do not appear in the urine or blood stream, the urobilinogen in the urine is increased rather than decreased, and evidences of the constitutional condition, usually an infection or an intoxication, responsible for the excessive hemolysis are commonly in evidence. In chronic hemolytic icterus even the urine contains no bile pigment, except occasionally after a marked hemolytic crisis. Hemoglobinuria occurs in some cases of hematogenous jaundice, but not as a rule, for unless free hemoglobin is present in the blood in very large amounts it is removed so rapidly by the liver that the threshold value of the kidneys for it is not exceeded.

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## CATARRHAL CHOLANGITIS

**(Catarrh of the Bile-ducts; Catarrhal Jaundice)**

**Definition.**—A catarrhal inflammation of the bile-ducts, more particularly of the lower end of the common duct, usually originating in the duodenum and causing an obstruction sufficient to produce jaundice.

**Etiology.**—Acute catarrhal cholangitis may occur at any age, but it is observed chiefly in childhood and early adult life. Males are more frequently affected than females. In the majority of cases the disease appears to be caused by the extension of a gastroduodenal catarrh resulting from

[1] Lancet, ii, 1896.

indiscretions in diet, chilling of the body or alcoholic excess. It is likely that the duodenitis is sometimes of an infectious nature, for epidemic occurrence is not uncommon. Outbreaks of catarrhal jaundice are usually circumscribed and of short duration. Less frequently the disease develops as a complication of one of the specific infections, such as pneumonia or typhoid fever, jaundice in these affections being in some cases frankly catarrhal and in other cases definitely toxemic and hemolytic.

Chronic cholangitis may be a sequel of the acute form, but more frequently it is observed in association with gall-stones or as a concomitant of some other disease of the liver, such as cirrhosis, carcinoma, or passive hyperemia the result of mitral disease.

**Morbid Anatomy.**—Opportunities for examining cases of acute catarrhal cholangitis post-mortem rarely occur. It is probable, however, that the changes consist of congestion, swelling, and increased secretion of viscid mucus at the lower end of the common bile-duct and in the duodenum surrounding the ampulla of Vater. The obstruction responsible for the jaundice may be due to swelling of the duct itself or, according to common belief, to blocking of the outlet of the duct by a plug of tenacious mucus. In certain cases of infectious origin it is possible that the catarrh, instead of extending upward from the duodenum, really begins in the minute intrahepatic ducts and spreads downward to the papilla.

Chronic catarrhal cholangitis may lead to dilatation of the ducts, with thickening and induration of their walls and eventually to pericholangitic fibrosis (obstructive biliary cirrhosis).

**Symptoms.**—The acute form usually begins with the symptoms of gastro-intestinal catarrh, such as coated tongue, foul breath, loss of appetite, nausea and perhaps vomiting. The bowels are, as a rule, constipated, but there may be diarrhea in consequence of the intestinal catarrh. In the course of a few days jaundice supervenes and gradually increases. Occasionally the digestive disturbance is so slight that it is overlooked by the patient, and the yellowness of the skin is the first symptom to attract attention. In the majority of cases the only other symptoms present after the first few days are the usual concomitants of simple obstructive jaundice, which have already been described (see p. 496). Bradycardia and pruritus are frequent, but not constant phenomena. Slight fever (100°–101° F.) is sometimes observed at the beginning of the attack, but it rarely lasts longer than two or three days. Ordinarily, neither the liver nor the gall-bladder is palpably enlarged or tender. A feeling of pressure, however, is sometimes experienced in the region of the liver. Bile that is aspirated from the duodenum after the administration of magnesium sulphate (see below) is, as a rule, darker, thicker and more viscid than normal, and turbid, and often contains pathogenic bacteria.

In the epidemic form the constitutional disturbance is sometimes more marked. Thus, there may be a rapid rise of temperature to 102° or 103° F., muscular pains, prostration, enlargement of the spleen, albuminuria, drowsiness or delirium, and even hemorrhages, the more severe examples closely simulating Weil's disease (Spirochætosis Icterohæmorrhagica), on the one hand, and acute yellow atrophy of the liver, on the other.

Uncomplicated cases of chronic catarrhal cholangitis are not common. Persistent jaundice, fluctuating in intensity from time to time, and loss of weight and strength, more or less pronounced, are usually the only symptoms. Not rarely the clinical picture so closely resembles that of biliary obstruction from some other cause, that a certain diagnosis can be reached only through exploratory operation or by observing the progress of the disease.

**Diagnosis.**—The diagnosis of the acute sporadic form is usually easy.

The sudden development of the disease in young otherwise healthy persons, the antecedent digestive disturbance, and the absence of pain, of severe constitutional symptoms, and of changes in the size of the liver are the characteristic features. Difficulty is sometimes encountered in the early stages of *acute yellow atrophy of the liver*, the jaundice being ascribed to simple catarrh until the occurrence of delirium, diminution of liver dulness, leucin and tyrosin in the urine, petechiæ and hemorrhages makes a revision of the diagnosis necessary. The epidemic form of catarrhal jaundice may closely simulate *Weil's disease*, but in the latter the specific spirochetes may sometimes be found in the blood and the blood is highly infectious for guinea pigs.

As it is not always possible to distinguish between chronic catarrh of the bile ducts and biliary obstruction resulting from gall-stones, chronic induration of the head of the pancreas or carcinoma, the advisability of making an exploratory incision should always be carefully considered when jaundice develops without obvious cause in middle-aged persons and persists after six weeks of rest and dietetic treatment. Generally speaking, jaundice developing gradually without pain and increasing steadily from week to week, while the gall-bladder increases in size, points to *compression of the common duct by a tumor or cicatricial tissue;* and persistent jaundice of varying intensity, preceded by colicky pains, and accompanied by ague-like paroxysms of fever, chill and sweat points to *impaction of a gall-stone in the common duct.*

**Prognosis.**—The outlook is usually good, the jaundice in the large majority of cases fading in from 3 to 6 weeks.

**Treatment.**—The treatment of the acute form is, for the most part, that of acute gastro-intestinal catarrh. Rest in bed and restriction of the nourishment to milk with lime-water or Vichy water or to light broth are indicated until the digestive disturbance has subsided. In the presence of nausea and vomiting abstinence from food for 24 or 36 hours is advisable. Even after the disappearance of the gastric irritation the nourishment should be simple and in moderate quantity. The bowels should be kept open by small doses of calomel, followed by a saline cathartic or by sodium phosphate, preferably in hot water. Bismuth subcarbonate or silver nitrate (1/4 grain—0.016 gm., in pill, three times a day) is sometimes of service. Hexamethylenamin has been recommended as a biliary antiseptic, but it is valueless. Hot, wet compresses over the upper part of the abdomen seem to be useful. In refractory cases the direct introduction of a 25 per cent. solution of magnesium sulphate into the duodenum through a duodenal tube, once a day, has been found efficacious.[1]

Chronic catarrhal jaundice requires similar treatment. Rest, a light, simple diet and the use of mild mercurial and saline aperients are indicated. Water drinking between meals should be encouraged. Alkaline mineral waters (Vichy, Vals, Hathorne, Vittel) may be used. Daily irrigation of the

[1] Meltzer (Amer. Jour. Med. Sci., April, 1917) showed that a 25 per cent. solution of magnesium sulphate, when introduced directly into the duodenum, relaxes the bile duct and permits of a free flow of bile from the gall-bladder to the duodenum. Lyon (Jour. Amer. Med. Assoc., Sept. 27, 1919; Amer. Jour. Med. Sci., April, 1920) has reported excellent results from the use of this solution in obtaining duodenal contents for diagnostic purposes and also as a means of treating inflammatory conditions of the biliary tract. The procedure is carried out in the fasting state. After the patient's stomach has been thoroughly rinsed and he has been placed on his right side with the hips slightly elevated, he is given a glass of water to drink, and then by *slow* swallowing the tube is allowed to enter the duodenum. When the latter is reached (15 to 45 minutes) 50 mils of a sterile 25 per cent. solution of magnesium sulphate are introduced. The first bile that is aspirated (2 to 10 minutes) is believed to be from the bile ducts. Presently bile from the gall-bladder is obtained.

colon with cold water (1–2 liters) has been recommended, but it is much less effective than the administration of a solution of magnesium sulphate through the duodenal tube. Pruritus may be relieved by a lotion of phenol, 2 drams (8.0 gm.) to the pint (0.5 L.), or of resorcin:

℞. Resorcinolis ..... ℥ss (6.0 gm.)
Sodii chloridi ..... ℥i (4.0 gm.)
Glycerini ..... f℥i (30.0 mils)
Liquoris calcis ..... q. s. ad Oj (500 mils).—M.

## SUPPURATIVE CHOLANGITIS

**Etiology.**—Suppurative inflammation of the bile-ducts is usually a sequel of cholelithiasis or obstruction of the ducts by tumors, damage to the biliary tract and stagnation of bile favoring pyogenic infection. Occasionally, the disease follows a general infectious process, such as pneumonia, influenza or typhoid fever. The usual inciting organisms are streptococci, staphylococci, pneumococci, colon bacillus, and typhoid bacillus. In the majority of cases the gall-bladder shares in the suppuration.

**Pathology.**—The ducts are swollen, dilated, and filled with pus. Abscesses, usually small, are frequently found at the extremities of the ducts or in the substance of the liver adjacent to the ducts. The liver itself is usually considerably enlarged and the seat of cloudy swelling and areas of necrosis. The suppurative process may extend to the portal vein, producing pylephlebitis, through the duct of Wirsung to the pancreas, leading to purulent pancreatitis, or to the peritoneum, setting up general peritonitis or localized peritoneal abscess; it may ulcerate through the diaphragm, causing empyema; or it may give rise to general septicopyemia.

**Symptoms.**—The most constant phenomena are a smooth uniform enlargement of the liver, increasing as the disease progresses, and the usual phenomena of septic infection—fever, chills, sweats, leucocytosis and rapid loss of flesh and strength. Jaundice is usually present and may be marked, but it often depends more on the antecedent disease than on the cholangitis itself. Pain in the hepatic region, variable in degree, is observed in the majority of cases. It may be due to the condition underlying the cholangitis, to stretching of the liver capsule, or to secondary peritonitis. Local tenderness is sometimes present even when pain is entirely absent. Enlargement of the spleen may also be noted.

**Diagnosis.**—A septic state with jaundice and a smooth enlargement of the liver in a patient who has already presented symptoms of cholelithiasis or of some other disease of the biliary tract, or who has recently suffered from a general infection, such as pneumonia or typhoid fever, is suggestive of suppurative cholangitis. In many cases, however, the clinical picture so closely resembles that of suppurative pylephlebitis or abscess of the liver that it is impossible to make an exact diagnosis. In the presence of progressive enlargement of the liver and septic phenomena, a history of acute appendicitis with pronounced enlargement of the spleen, but with inconspicuous jaundice, is in favor of *pylephlebitis;* whereas a history of dysentery with neither splenic enlargement nor jaundice points strongly to *heptic abscess.* If in addition there is a distinct tumor with edema of the abdominal wall the diagnosis of abscess is almost certain. It must be remembered, of course, that combinations of these conditions may occur in the same patient.

**Prognosis and Treatment.**—The prognosis is very grave, although recovery may occur if free drainage of the gall-bladder and bile-ducts can be accomplished and the cause removed at an early stage. Medical treatment is merely palliative.

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## ACUTE CHOLECYSTITIS

Inflammation of the biliary tract may begin either in the gall-bladder or in the ducts and then spread from one to the other, the initial lesion in some cases persisting and in other cases subsiding after the extension has occurred. Not infrequently, however, the inflammation is confined throughout to the gall-bladder or to the ducts.

**Etiology.**—The occurrence of acute cholecystitis is favored by all factors that lessen the resistance of the gall-bladder or interfere with the free flow of bile. The immediate cause of the inflammation is microbic infection.

In a large proportion of cases the disease follows cholelithiasis or occurs as an acute exacerbation of a chronic non-calculous cholecystitis. Less frequently it accompanies or follows one of the general infections, especially typhoid fever, and still less frequently it is secondary to a focus of infection in the alimentary canal, such as appendicitis or peptic ulcer.

Occasionally, it develops after tonsillitis or occurs in association with some equally remote local infection. The association with appendicitis, which is by no means rare, has attracted much attention. It is possible that the two conditions may develop simultaneously, the infection emanating from a single focus, or that one condition may be primary and the other secondary.

The common infective agents are the colon bacillus, the typhoid bacillus, streptococci and staphylococci. In many cases more than one organism is present. Much importance has been attached to the colon bacillus, but doubtless this prolific organism sometimes crowds out others of greater pathogenic significance. In the later stages of the disease bacteria may be absent from the bile and only present in the tissues of the gall-bladder. The channel of invasion is probably in most cases the hepatic artery (general circulation), although it may be the portal vein or the bile-ducts.

**Pathology.**—The inflammation is usually of the catarrhal type, but depending on the virulence of the infection, the resistance of the organ, and the degree of obstruction to biliary drainage, it may be suppurative, phlegmonous, gangrenous or membranous. According to Aschoff and Bacmeister frank suppuration only occurs when the cystic duct is occluded by stone or inflammatory edema.

In catarrhal cholecystitis the gall-bladder is distended and tense, the wall is swollen, the mucous membrane is congested and sometimes slightly ulcerated, and the peritoneal coat is dull and in severe cases attached to adjacent structures by a layer of fibrin. The cystic duct is often partially closed by swelling of the mucosa or by cicatricial thickening that has resulted from previous attacks of inflammation. The adjacent lymph-nodes, especially those in the portal fissure, are enlarged. The gall-bladder is usually filled with turbid bile-stained fluid, but in long-standing cases it may contain pus (*chronic empyema of the gall-bladder*). Gall-stones are sometimes present, usually, however, as the result of previous attacks or of an underlying chronic cholecystitis.

In the more severe cases the changes in the wall of the gall-bladder vary

from those of acute septic inflammation to those of advancing gangrene. The viscus is usually distended and attached by adhesions to contiguous structures and its walls are edematous, friable, and often infiltrated with pus. The color may be reddish purple, dark green, or even black. The cystic duct is closed and may be blocked by a calculus. The contents are dark in color, and purulent or hemorrhagic. As contrasted with chronic empyema of the gall-bladder, acute suppurative or phlegmonous cholecystitis rapidly proceeds, as a rule, to ulceration, necrosis and perforation of the wall of the gall-bladder and to fatal peritonitis. In very rare instances, usually of calculous cholecystitis, the gall-bladder becomes lined with a false membrane (membranous cholecystitis), which subsequently may be discharged in the stools with the symptoms of gall-stone colic.

**Symptoms.**—The symptoms of mild cholecystitis are usually ascribed to functional gastric disturbance as they comprise merely those of indigestion with flatulence and a sensation of tightness, weight or oppression in the region of the stomach. In more pronounced attacks there may be, in addition, regurgitation or vomiting, pain in the right hypochondrium, tenderness under the right costal arch, distention of the gall-bladder, fleeting rigidity of the right rectus, and, perhaps, slight fever. The pain may be dull and continuous, or severe and paroxysmal, like that of gall-stone colic. Jaundice is rarely present unless there is an associated cholangitis or some obstruction in the bile ducts. General enlargement of the liver is also exceptional in uncomplicated cases, but in acute attacks supervening on chronic cholecystitis palpation sometimes reveals a tongue-like elongation of the right lobe (Riedel's lobe), which may readily be mistaken for a distended gall-bladder.

In severe attacks (suppurative, phlegmonous, or gangrenous cholecystitis) pain, often intense and of a colicky character, is the first symptom. It is usually felt in the right hypochondrium, but it may be referred to the epigastrium or even to the region of the vermiform appendix. With the pain there are the usual symptoms of localized or diffuse peritoneal infection, namely, rapid pulse, thoracic breathing, fever, polymorphonuclear leucocytosis, persistent vomiting, prostration, marked tenderness and rigidity, especially over the right side of the abdomen, and increasing tympanites. Jaundice may or may not be present. The bowels are usually unaffected but occasionally, as in appendicitis, symptoms of intestinal obstruction supervene, owing to the paralyzing effect of the peritonitis. The gall-bladder is sometimes palpable as a tense pear-shaped tumor, but it may be shrunken from antecedent attacks of inflammation, and even if enlarged, it may escape detection owing to abdominal rigidity or distention.

**Course and Events.**—Mild attacks usually subside under appropriate treatment within a week or ten days. Doubtless, in some cases the process terminates in complete resolution, but far more frequently it passes into chronic cholecystitis or, gives rise to pericholecystic adhesions, which in turn may cause various functional disturbances of the stomach or even pyloric obstruction and gastrectasis. Chronic cholecystitis may be accompanied by an effusion of pus (chronic empyema of the gall-bladder), although, as a rule, it continues as a catarrhal process, marked by recurring acute attacks and frequently leading to cholelithiasis (calculous cholecystitis) and not rarely to induration and atrophy of the gall-bladder (chronic fibrous or atrophic cholecystitis). The more severe forms of acute cholecystitis, if left to themselves, usually prove fatal within a few days, diffuse peritonitis ensuing either from direct extension of the infective process or from actual rupture of the gall-bladder. In some cases perforation of the gall-bladder

leads to the formation of a local abscess (subphrenic abscess), which may subsequently discharge into some adjacent cavity or viscus.

**Diagnosis.**—The diagnosis of acute cholecystitis is usually easy, but it may be difficult or impossible. Nausea and vomiting, pain and tenderness in the region of the gall-bladder, and the presence of a smooth, round, tense tumor near the liver, even if no history of gall-stones can be obtained, will, of course, at once suggest the lesion. Ordinarily, *appendicitis* can be excluded by the location of the pain and tenderness, but mistakes are very likely to occur if the gall-bladder is much elongated or the appendix lies behind the cecum and extends toward the liver. Often it is quite impossible to differentiate non-calculous cholecystitis from calculous cholecystitis. In the more severe cases with signs of acute peritonitis on the right side of abdomen one must exclude appendicular abscess high up, pyonephrosis, suppurative pancreatitis, and subphrenic abscess from perforated gastric or duodenal ulcer. Unless a suggestive history is obtained or there are signs clearly indicating inflammatory enlargement of the gall-bladder the nature of the case may admit only of conjecture.

**Treatment.**—The treatment of acute cholecystitis is essentially that of acute cholangitis. Rest in bed, and a diet of light, easily digested food are indicated. Hot or cold compresses may be applied to the region of the gall-bladder. If the pain is severe it may be necessary to give morphin subcutaneously. Gastric sedatives, such as bismuth subcarbonate and cerium oxalate, should be used to control vomiting. As soon as it can be tolerated, a moderate dose of calomel may be given and followed by a saline cathartic. Alkaline waters, such as Carlsbad, Vittel, or Vichy, may be used freely. Daily rectal injections of 1 or 2 quarts of cool water or lavage of the duodenum with a solution of magnesium sulphate (see p. 499) may be employed to favor the escape of the infected bile. If the inflammation does not promptly subside under medical treatment or if it is characterized by severe symptoms of general infection an operation, which should include free drainage of the biliary tract, should be undertaken without delay.

## CHRONIC CHOLECYSTITIS

**Etiology.**—Chronic inflammation of the gall-bladder may be a sequel of acute cholecystitis or it may be chronic from the beginning. In the majority of cases (about 70 per cent.) the disease is associated with cholelithiasis, although it probably nearly always precedes the stone formation and is the cause of the latter rather than its effect. The immediate cause of the inflammation is an attenuated infection, and the predisposing factors are those which favor stagnation or retention of bile, such as sedentary habits, overeating, tight lacing, pregnancy, obesity, intestinal stasis, and obstruction of the bile-ducts. Although it is possible that the infecting agents may sometimes reach the biliary tract directly from the intestine, clinical and experimental studies indicate that they usually enter the liver by way of the hepatic artery (general circulation) or the portal vein, and in traversing the liver undergo such a reduction in virulence that they produce a chronic catarrh of the gall-bladder rather than an acute inflammatory process. Much importance attaches to typhoid infection. Typhoid bacilli are almost constantly present in the gall-bladder in typhoid fever, and sometimes remain there for an indefinite period after recovery, being intermittently or continuously discharged into the bowel ("typhoid carriers") and not rarely exciting in the

gall-bladder itself acute or chronic inflammation after an interval of months or years. In many cases of chronic cholecystitis the infection apparently has a local origin, the organisms gaining entrance to the circulation, through a lesion of the stomach, the bowel, the appendix, the tonsil, or even some more remote structure.

**Pathology.**—The changes are sometimes so slight that the diagnosis cannot be definitely established postmortem until the gall-bladder is opened and the mucous membrane is subjected to a thorough examination. According to Mayo, the gall-bladder in some cases is large, blue and filled with foul-smelling-pus, and in others, thick-walled, whitish, and filled with thick, tarry bile, with a large admixture of mucus. Gall-stones may or may not be present. The adjacent lymph-nodes are almost always enlarged and in long-standing cases may be calcareous. The mucous membrane is often covered with yellow specks ("strawberry gall-bladder"), which represent villi denuded of epithelium and stained with bile. Occasionally fine grains of calculous matter are found imbedded in the mucous membrane even when no stones are present. Ultimately, in many cases the gall-bladder becomes shrivelled and thickened from the contraction of the inflammatory tissue and not rarely it undergoes calcification. Secondary lesions, especially adhesions between the gall-bladder and adjacent structures, acute or chronic pancreatitis, and biliary cirrhosis, make their appearance, sooner or later, in a large proportion of cases.

**Symptoms.**—The symptoms may be merely those of chronic indigestion accompanied by a sensation of weight or oppression in the upper part of the abdomen and flatulence. In many cases, however, there are certain suggestive features, such as the tendency of the indigestion to occur in attacks at irregular intervals, sudden in onset and termination, and without any very definite cause; the frequent appearance of the discomfort at night, the failure of food to afford relief, the pronounced flatulence and belching, the presence of slight tenderness under the right costal border, and of transient rigidity of the right rectus muscle.

Less frequently the attacks are accompanied by some distention of the gall-bladder, chilly sensations, a slight rise of temperature and a faint icteroid tinge of the scleræ or skin. In some instances, especially after the formation of pericholecystic adhesions, there are attacks of pain closely simulating biliary colic, even though gall-stones are absent. Not rarely in long-standing cases the digestive disturbances are accompanied by palpitation and precordial oppression, and occasionally symptoms referable to the heart completely overshadow those pertaining to the gall-bladder.[1]

Pronounced jaundice is not a feature of uncomplicated cases, but it may occur in the event of an accompanying cholangitis, impaction of a stone in the common duct, or compression of the common duct by adhesions, enlarged lymph-nodes, or indurative swelling of the pancreas. The degree of gastric acidity varies in different cases, but in the later stages it is more common to have low than high acidity. Lyon's method of utilizing the duodenal contents for study after the direct introduction of magnesium sulphate into the duodenum promises to be helpful in diagnosis (see p. 499). Occasionally, roentgenographic examination yields important circumstantial evidence, even when stones are not present in the gall-bladder. Thus, fixation of the duodenum or pylorus by adhesions, Riedel's lobe of the liver, and gastrospasm are sometimes shown and are suggestive if other roentgenographic signs, laboratory analyses, and the anamnesis make the diagnosis of peptic ulcer improbable.

[1] See report of 13 cases by Babcock, Jour. Amer. Med. Assoc., lii, 1909.

**Diagnosis.**—In all cases of persistent indigestion, especially in persons in middle or later life, the possiblity of chronic cholecystitis should be considered and careful search instituted for definite signs of infection in the gall-bladder. If these are absent the diagnosis cannot be made with certainty. In the differential diagnosis one must consider gastric or duodenal ulcer, carcinoma of the gall-bladder, liver or adjacent viscera, the various gastric neuroses, and chronic appendicitis. The discovery of gall-stones in the stools and the occurrence of clearly defined shadows in the roentgenogram are the only positive evidence that cholecystitis is of the calculous variety. Negative findings in these respects, however, by no means exclude the possibility of cholelithiasis.

**Treatment.**—An important object of treatment is to promote a free flow of unirritating bile, and to accomplish this dietetic and hygienic regulations demand the first consideration. The diet should be mixed, bland, easily digestible, and generous rather than meagre. Strong soups, heavy gravies, potted and preserved meats, high game, greasy pastry, overripe cheese, much sweets, highly seasoned dishes and alcoholic beverages of all kinds should be avoided. The food must be thoroughly masticated and should be taken neither too hot nor too cold. In some cases, if the gastric digestion is well maintained, it is advantageous to give the food in smaller quantities and at comparatively short intervals. A light meal at bedtime has been specially recommended by Kehr. Frequent feeding may prove harmful, however, if there is atony of the stomach with impairment of gastric motility. An important point is the supply of sufficient water to dilute the body fluids and to remove from the alimentary canal irritating products of digestion. A glass of hot Carlsbad water, or if this is not well borne, of cool plain water, may be taken between meals and at bedtime, and before or after rising. To increase still further the supply of fluid without interfering with digestion a rectal injection of two quarts or more of cool water every few days is often beneficial. Exercise in the open air, regulated according to the patient's needs and habits, unquestionably has a salutary effect, provided of course, there are no acute symptoms. Systematic deep breathing is also useful in overcoming the tendency to portal and biliary stasis. Constriction of the upper part of the abdomen by corsets or other articles of dress must be avoided. Freedom from worry and mental strain rarely fails to afford some relief.

Digestive disturbances and constipation should receive appropriate treatment. If necessary laxatives should be used. Sodium phosphate, Carlsbad salt, or Rochelle salt may be added to the water which is drunk before breakfast and between meals. The natural mineral waters probably have no special advantages, although those of Carlsbad and Vittel have a high reputation. An occasional course of calomel, in fractional doses, is often useful. Among special remedies, sodium succinate—5–10 grains (0.3–0.6 gm.) after meals—is worthy of trial. Hexamethylenamin, up to a total of 30 grains (2.0 gm.) a day, has been recommended for its antiseptic properties, but it is doubtful whether it yields enough formaldehyde in the biliary passages to be effective. Sodium glycocholate—5 grains (0.3 gm.) after meals—has a cholagogue action, and may be of value in some cases. In the milder cases the introduction of magnesium sulphate by tube into the duodenum, as recommended by Lyon (see p. 499), may aid in draining the gall-bladder. If the patient's circumstances will permit a course of treatment at Carlsbad, Vittel, Contrexville, or Vichy in Europe, or at Bedford or Las Vegas Hot Springs in America may be recommended with some degree of confidence. An extended visit at one of these resorts is often followed by

marked improvement and occasionally by permanent relief. The benefit probably depends as much upon change of air and scene, genial surroundings, freedom from worry, and regular hours as upon the action of the waters themselves. If no benefit accrues from medical treatment after a thorough trial surgical aid should be invoked without further delay, otherwise serious complications (see p. 508) are likely to supervene. The mortality of operation in simple cases and in expert hands is less than 2 per cent.

## CHOLELITHIASIS

(Gall-stones)

**Etiology.**—Statistics taken from the postmortem records of American and European hospitals indicate that from 3 to 10 per cent. of all patients have gall-stones. While these figures may give a fair estimate of the frequency of gall-stones in sick persons, they are probably in excess of the truth if applied to the population at large. Perhaps 1 or 2 per cent. would be a more correct estimate of the general incidence. The percentage is apparently higher in central Europe than in England or America and much lower in India and other Asiatic countries. Negroes are somewhat less frequently affected than white persons. No period of life is exempt, but the large majority of cases are observed in persons over 35. The percentage incidence is apparently highest after 55 or 60, but doubtless in very many cases stones found in late life have been formed at a much earlier period. Gallstones are uncommon before 20 and are exceptional in childhood and infancy. They are of frequent occurrence in children suffering from chronic family jaundice, but this condition is comparatively rare. Women are more frequently affected than men, the ratio being about 3 to 1. The influence of heredity, upon which Bouchard, Chauffard, and other French writers have laid much stress, is by no means proved. All factors which interfere with a free flow of bile dispose to cholelithiasis. Among these factors may be mentioned sedentary habits, errors in diet, tight lacing, intestinal stasis, relaxation of the abdominal muscles, obesity, pregnancy, abdominal tumors, visceroptosis, and stenosis of the bile ducts, however produced. Pregnancy and pelvic neoplasms are especially important. According to Schroeder[1] and Mayo[2] 90 per cent. of married women who have gall-stones have borne children and 90 per cent. of these women (Mayo) identify the beginning of the symptoms with some particular pregnancy. In 1066 abdominal sections for pelvic disease, Peterson[3] found gallstones in 12.6 per cent. of the cases.

The immediate cause of cholelithiasis in the large majority of cases is a chronic inflammation of the gall-bladder excited by typhoid bacilli, colon bacilli, or streptococci, which have been carried to the liver through the hepatic artery (general circulation), portal vein, or, possibly in some instances, the bile-ducts, and which have not been destroyed in traversing the liver, but in consequence have undergone a marked reduction in virulence. The etiologic importance of typhoid fever has come to be generally recognized, but other infections, especially focal streptococcus infections, have been shown to be equally potent. Streptococci, typhoid bacilli, and other bacteria are frequently found in the center of gall-stones. Conditions favorable to

[1] Quoted by Naunyn, Sholelithias, 1896.
[2] Jour. Amer. Med. Assoc., April 8, 1911.
[3] Surg., Gynec. and Obstet., 1915, xx, No. 3.

the production of gall-stones experimentally in animals are the employment of an attenuated virus and the establishment of some impediment to the escape of bile.

While infection of the gall-bladder is undoubtedly the chief cause of cholelithiasis, Aschoff and Bacmeister[1] seem to have proved that at least one form of gallstone (cholesterol) can be formed in sterile bile if the flow is hindered. This view has been accepted by Kehr, Chauffard, and even by Naunyn[2] (Ewald), who was the first to teach that infection was essential to the precipitation of cholesterol. What the factor is which in addition to stagnation favors the formation of calculi in non-infected gall-bladders has not been determined. Chauffard,[3] Kehr, and others believe that it is some disturbance of metabolism, possibly of dietetic origin, which results in hypercholesterolemia, although high concentrations of cholesterol in the blood (normally, 150 to 200 mg. per 100 mils of blood) may be found in many conditions, and do not seem to be especially significant (Reiman and Magoun,[4] Gorham and Myers,[5] Denis,[6] Schnabel[7]).

**Classification of Gall-stones.**—The chief constitutents of gall-stones are cholesterol and the calcium salts of the bile pigments, especially bilirubin-calcium. Calcium carbonate is also present in some cases and is rarely a predominant constituent. (1) *Common or mixed gall-stones* are composed of cholesterol and bilirubin-calcium in various proportions. They may be single, large and round, but, as a rule, they are multiple, facetted in their apposed aspects, and not larger than a pea or a small cherry. The external color varies according to the predominance of cholesterol or bilirubin-calcium from pale yellow to greenish-black. Some of them have a hard laminated mantle and a relatively large, soft, pigmented nucleus, but others are laminated and firm throughout. (2) *Pure cholesterol stones* are usually single and oval, pale yellow, translucent, and without facets. They vary in size from that of a cherry to that of a pigeon's egg, and on section are crystalline, but not stratified. (3) *Bilirubin-calcium stones* are multiple, of small size—from that of a grain of sand to that of a small pea—and form irregular brownish-black concretions, of wax-like consistence when fresh but hard and brittle when old. They are formed usually in the intrahepatic ducts, but are frequently carried to the gall-bladder, where they may serve as nuclei for mixed calculi. (4) *Calcium carbonate stones* are small and are rarely found in man.

**Mode of Formation of Gall-stones.**—Gall-stones usually originate in the gall-bladder, although they are frequently found in the larger ducts. Bilirubin-calcium stones only are formed in the intrahepatic ducts. In the gall-bladder inflammation leads to degeneration and desquamation of the epithelium. With the epithelium there is thrown off a large amount of undissolved cholesterol, which collects around masses of detached cells, agglutinated bacteria, or small granules of bilirubin-calcium. Once formed the concretion grows by the further addition of cholesterol or bilirubin-calcium, or both. The formation of bilirubin-calcium, the second important constituent of gall-stones, depends upon a desquamative inflammation of the biliary passages. As pointed out by Naunyn, the disintegrating epithelium furnishes an excess of calcium salts and these in the presence of the albuminous exudation of the inflammatory process interact with the bilirubin of the bile to form precipi-

[1] Die Cholelithiasis, 1909.
[2] A Treatise on Cholelithiasis, Syden. Soc. Trans., 1896.
[3] Leçons sur la Lithiase Biliare, 1914.
[4] Surg., Gynec. and Obst., Mar., 1918.
[5] Arch. Int. Med., 1917, xx, 4.
[6] Jour. Biol. Chem., 1917, xxix, 93.
[7] Amer. Jour. Med. Sci., 1920, clx, No. 3.

tated bilirubin-calcium. Any interference with the flow of bile disposes to infection, or if the latter has already developed tends to prolong it by hindering the escape of bacteria into the intestines.

While it seems to have been established that pure cholesterol stones may be produced in the absence of infection, the nature of the process that brings about the precipitation of the cholesterol is not definitely known. However, a pure cholesterol stone may excite inflammation and in consequence become enclosed in a mantle of laminated deposit.

**Pathology.**—In the large majority of cases the stones are found in the gall-bladder alone; less frequently they are found in the large ducts; and occasionally they are found in the intrahepatic bile-passages. Stones found in the cystic duct or common bile-duct have usually, but not invariably, been derived from the gall-bladder, their migration probably having been effected by an acute inflammatory condition (acute cholecystitis) which distended the viscus with exudation or excited in it abnormally vigorous contractions. Stones found in the intrahepatic passages have usually been formed *in situ*. Gall-stones vary in number from solitary concretions to scores, hundreds, or even thousands, and in size from that of a millet seed (biliary gravel) to that of a hen's egg. Their size and shape have some relation to their number, single calculi usually being large and round or ovoid, and multiple calculi, comparatively small, and from growth while in contact, rather than from mutual attrition, cuboidal or polyhedral and facetted. Stones in the ducts may be cylindrical or in rare instances branched.

Secondary changes due to infection or to the mechanical action of the gall-stones themselves are frequently observed in the gall-bladder and adjacent structures. Cholecystitis, acute or chronic, catarrhal or suppurative, and progressing in some cases to ulceration and perforation, and in others to sclerotic thickening of the wall of the gall-bladder, is especially common. Although gall-stones are usually the result of a mild catarrhal inflammation their presence favors fresh infection and hence the occurrence of active, even of suppurative or gangrenous cholecystitis. In long-standing cholelithiasis the gall-bladder is frequently small and firmly contracted about the concretions (atrophic sclerosing cholecystitis). Ulceration not rarely leads to perforation of the viscus and the discharge of the stones in one of several directions. The most common routes are externally through the abdominal wall, into the peritoneum, into the duodenum, and into the colon. But the opening may also take place into the pleura and lung, stomach, different parts of the biliary passages, urinary tract, portal vein or retroperitoneum. Rupture into the hepatic artery may also occur, but is very rare. Rupture into the peritoneum results in circumscribed peritoneal abscess or in acute diffuse peritonitis, according as the general cavity of the peritoneum has or has not been shut off by adhesions. Perforation of the gall-bladder is sometimes followed by permanent fistulæ between the biliary passages and other viscera or the outside of the body, but in the majority of cases the openings are closed spontaneously by adhesions. Cicatrization following ulceration sometimes results in diverticula or in hour-glass contraction of the gall-bladder. Even in the absence of ulceration and perforation, inflammation of the gall-bladder very frequently spreads to the peritoneum leaving as a consequence adhesions with the viscera or abdominal wall. All grades of these adhesions are observed. In mild cases only slender threads of connective tissue are found in the region of the gall-bladder ("spider webs"); in extreme cases the gall-bladder, or a calcareous nodule representing it, is found deeply imbedded in a mass of solid cicatricial tissue.

Lesions similar to those observed in the gall-bladder in cholelithiasis—

inflammation, ulceration, perforation, etc.—also occur in the large bile-ducts. Stricture of the ducts, especially of the cystic duct, is not an uncommon sequel of ulceration. Persistent obstruction of the cystic duct by a calculus may result in one of three conditions: (1) Distention of the gall-bladder with clear or bile-stained fluid—dropsy of the gall-bladder (hydrops vesicæ felleæ)—the excess of fluid probably being due to a catarrh of the viscus; (2) after temporary distention, a gradual shrinkage of the gall-bladder, until finally all trace of a cavity is lost; or (3) phlegmonous cholecystitis (empyema of the gall-bladder). Occasionally a gall-bladder may be so large as to be mistaken for an ovarian cyst. Distention of the gall-bladder with fluid or a large collection of stones is sometimes associated with a pronounced elongation of the right lobe of the liver, which is known as Riedel's[1] linguiform lobe. Obstruction of the common bile-duct by gall-stones usually occurs at the lower end of the duct near the duodenum or in the ampulla of Vater. The calculus may be firmly impacted or it may be loose (floating) and exert a ball-valve action. Not rarely several stones are present. Persistent obstruction leads to dilatation of the ducts and finally to biliary cirrhosis of the liver. The gall-bladder is, as a rule, contracted rather than dilated (Courvoisier), probably because of inflammatory thickening and cicatrization, the consequence of persistent infection.

Pancreatitis, acute or chronic, is a frequent accompaniment of cholelithiasis, especially of calculi in the common bile-duct. Infection may be carried to the pancreas through the lymphatics or by way of the common bile-duct and Wirsung's duct, the two ducts often terminating in a single orifice; or if the outlet of the papilla of Vater is completely closed by a calculus an extensive necrosis of the gland may occur in consequence of the retrojection of bile directly into the pancreatic duct (Opie). Inflammation of the bile-ducts or even compression of the portal vein by stones in the gall-bladder or bile-ducts rarely gives rise to pylephlebitis. Large concretions entering the bowel occasionally cause intestinal obstruction. When this accident occurs the entrance of the stone into the bowel has been effected in the vast majority of cases through a fistulous opening between the gall-bladder and the duodenum, and the site of the obstruction is, as a rule, in the lower end of the ileum near the ileocecal valve. A stone which enters the duodenum through the natural passage—the common bile-duct—almost invariably passes through the bowel without difficulty, unless, as in exceptional cases, it becomes enlarged in transit or is arrested at some abnormal point of constriction. Another sequel of gall-stones that is by no means uncommon is carcinoma of the gall-bladder or biliary passages. Schroeder found carcinoma present in 14 per cent. of 141 cases of cholelithiasis; Keay[2] in 11 per cent. of 149 cases; Rolleston[3] in 4.1 per cent. of 242 cases, and Mayo in 2.25 per cent. and Riedel[4] in 7.4 cases requiring operation.

**Symptoms.**—Contrary to the belief formerly prevailing that gall-stones in the majority of cases cause no appreciable disturbances, it is now generally recognized that they rarely fail to produce symptoms, but that these are commonly referred to the stomach. The earliest manifestations are, as a rule, the result of chronic cholecystitis (see p. 504) and may be altogether equivocal. Suggestive features are attacks of indigestion with pronounced flatulence, occurring at irregular intervals, suddenly, without any very definite cause, and often nocturnal. Even more significant in some of the attacks

[1] Riedel, B. M. C. L.: Erfahrungen über die Gallensteinkrankheit mit und ohne Icterus, Ed. 8, Berlin, 1892, p. 11.

[2] Keay, J. H.: Medical Treatment of Gall-stones, Phila., 1902, p. 67.

[3] Rolleston, H. D.: Diseases of the Liver, Phila., 1905, p. 737.

[4] Zeitft f. aerztliche Fortbildung, April 1, 1906.

is the occurrence of stabbing pain at the right costal margin upon deep breathing, slight tenderness and rigidity over the region of the gall-bladder, a mild rigor, or a faint icteroid tinge of the conjunctivæ. Conspicuous jaundice is absent throughout in a large proportion of cases (80 per cent., Kehr;[1] 34 per cent., Kelly;[2] 75 per cent., Graham[3]). In the intervals between the attacks the appetite and the digestion are often good, at least for a long period. Estimations of the gastric acidity yield variable results. In many cases, however, the acidity is normal (Ewald, Billings). Enlargement of the gall-bladder, appreciable on palpation, is sometimes observed, and in very rare instances crepitation can be elicited.

*Biliary Colic.*—The symptom most characteristic of cholelithiasis is colic. This is present, however, in but a minority of cases, although dull pains of various kinds are rarely altogether absent. As regards the cause of biliary colic the weight of opinion supports the view that an active infection and consequent inflammation of the biliary tract resulting in spasmodic efforts of the gall-bladder to expel its contents is the important factor. Pains of the greatest intensity usually signalize the propulsion of a stone into the cystic duct and cease when the stone escapes into the bowel, enters a wider part of a duct, or slips back into the gall-bladder. In some instances the attacks of colic may be determined by errors in diet, exposure to cold, or jolting of the body, but more frequently they occur without an obvious cause. The pain is usually sudden in onset and very severe; in fact it is often so agonizing that the patient moans and throws himself about vainly seeking relief by change of posture. As a rule, it is felt first in the epigastrium or right hypochondrium, and then passes through to the back, rarely as high as the right shoulder. Sometimes it begins in the back and afterwards spreads to the right hypochondrium, and occasionally after the formation of adhesions it is experienced chiefly in the left hypochondrium. It rarely radiates below the umbilicus. The pain may pass off in a few minutes; usually it lasts several hours, and occasionally it continues with remissions for days. In many cases it ceases as suddenly as it came. As a result of the intense suffering there is often marked prostration, with profuse clammy perspiration and a weak, rapid pulse, and rarely the patient falls into a state of actual collapse or syncope. Vomiting nearly always occurs and usually affords some relief, but it may persist and so increase the prostration. The material vomited consists chiefly of bile-stained mucus. A chill with or without a subsequent rise of temperature (100° to 104° F.) occurs in many cases; indeed, it is more common in biliary colic than in any other condition causing recurring attacks of abdominal pain. Jaundice, the result of temporary occlusion of the common bile-duct or of concomitant cholangitis, may appear toward the end of a paroxysm and is very significant, but as it is present in less than two-thirds of the cases, its absence is unimportant. Tenderness over the region of the gall-bladder is often noted and occasionally there is slight enlargement of the liver. Palpitation and precordial discomfort are rarely complained of and a systolic murmur over the apex is sometimes present.

The detection of biliary calculi in the stools after an attack of colic is, of course, positive evidence of cholelithiasis, but their absence has no diagnostic significance. According to Kehr search for them is successful in not more than 25 per cent. of the cases. The stone may not have escaped into the bowel, but may have slipped back into the gall-bladder, or may have remained

[1] Medical and Surgical Treatment of Gall-stone Disease, 1906.
[2] Amer. Jour. Med. Sci., 1906, cxxxii.
[3] Colorado Medecine, 1918, xv.

in one of the ducts; it may have been retained for a time in the intestines; it may have undergone disintegration; or the colicky pain may not have been excited by the passage of stone, but may have been the result simply of inflammatory irritation and distention of the gall-bladder. The best method of searching for calculi is to wash the stools through a fine sieve after diluting them with a two per cent. solution of formalin.

The interval between the attacks varies; it may be weeks, months, or years; occasionally there is only one attack. The occurrence of a number of mild seizures in quick succession usually indicates that a stone is slipping to and fro in either the cystic or the common duct.

*Obstruction of the Cystic Duct.*—Permanent obstruction of the cystic duct by a calculus may result in dropsy of the gall-bladder, cholecystitis (catarrhal, suppurative, or gangrenous), or cirrhotic atrophy of the gall-bladder. A distended gall-bladder appears as a smooth tense tumor projecting from the margin of the liver, pear-shaped with the base downward, and usually movable with respiration. Pain, dull or colicky, may be present, but it is often absent. Jaundice is absent in the large majority of cases; it may occur, however, in consequence of concomitant cholangitis or of compression of the common bile-duct by swollen lymph-nodes, adhesions, or even a large stone in the cystic duct.

*Obstruction of the Common Bile-duct.*—A stone in the common bile-duct may become fixed or may remain free and movable. In either case jaundice, usually with remissions, is the most constant symptom, although the obstruction may continue for years without it. According to Kehr, Moynihan, Mayo and others it is absent in from 25 to 30 per cent. of the cases. Even when the jaundice is pronounced bile can usually be aspirated from the duodenum by means of the Einhorn tube, showing that the obstruction is not often complete. In many cases, especially if the stone is movable and exerts a ball-valve action, there are recurring attacks at irregular intervals of chill, fever (103°–105° F.) and sweating, closely resembling malaria (Charcot's[1] intermittent hepatic fever), and probably due to infection of the common bile-duct, which has a relatively rich lymphatic supply. During the attacks, which often last several days, there are usually colicky pains in the epigastrium or right hypochondrium, digestive disturbances, tenderness in the region of the liver, leucocytosis, and deepening of the jaundice or the occurrence of jaundice if it has not already existed.

Occasionally both jaundice and pain are absent and the ague-like paroxysms are the only feature. The gall-bladder is usually contracted, whereas in malignant disease and other conditions causing obstruction of the common bile-duct it is, as a rule, distended (Courvoisier's[2] law). The attacks may continue for months or even years, and the patient in the intervals may be fairly well; eventually, however, pancreatitis, suppurative inflammation of the bile-ducts or biliary cirrhosis of the liver is likely to supervene.

**Complications and Sequels.**—With few exceptions these have been referred to under the head of Pathology (see p. 508). The most common complications or sequels are the various forms of cholecystitis and cholangitis, pericholecystic adhesions, pancreatitis, especially the chronic form, circumscribed peritoneal abscess, acute diffuse peritonitis, and chronic myocardial degeneration. Among the less frequent complications or sequels may be mentioned obstructive biliary cirrhosis, carcinoma of the gall-bladder or biliary passages, intestinal obstruction, biliary fistulæ, diverticula or hour-glass constriction of the gall-bladder, stricture of the cystic or of the common bile-duct, abscess of the liver and pylephlebitis.

[1] Leçons sur les Mal. du foie et des Voies biliares, 1877.
[2] Path. und Chirurg. der Gallenwegen, 1890.

Degeneration of the myocardium with relative insufficiency of the mitral valve is by no means uncommon. It is probably a direct result of the infection in the biliary tract. Occasionally, symptoms referable to the heart completely overshadow those arising from the cholelithiasis. Intestinal obstruction is usually the result of impaction of the bowel by a calculus, but it may be due, as Mayo Robson[1] has shown, to paralysis of the bowel from local peritonitis, to volvulus from violent colic, or to compression of the bowel by adhesions. Finally, calculous cholecystitis, like other focal infections, has the power to initiate or perpetuate arthritis.

**Diagnosis.**—The diagnosis of cholelithiasis can be made with absolute certainty only by the discovery of characteristic concretions in the stools after an attack of colic or by the appearance of distinct, sharply defined shadows in the roentgenogram, but the diagnosis of chronic cholecystitis with a strong probability of gall-stones can be made in the large majority of cases from the history, especially the early course of events before complications have arisen, and the results of a careful physical examination. The important indications are stated on p. 509. Jaundice is not at all necessary to a diagnosis and its absence in doubtful cases is without significance. Even if the symptoms are somewhat atypical, their occurrence during pregnancy or soon after labor is always suggestive. The frequency with which gall-stones can be demonstrated by the roentgen-ray is a debatable question. Probably irrefutable evidence is obtained in not more than 40 or 50 per cent. of the cases. The great danger is in faulty interpretation, as suspicious shadows are very common. Only calculi comparatively rich in calcium are well shown, and therefore little importance is to be attached to negative findings.

The conditions most likely to be confused with cholelithiasis are peptic ulcer, carcinoma of the stomach, pancreas or biliary passages, chronic appendicitis and chronic pancreatitis.

In *peptic ulcer* there are recurring attacks of pain, vomiting, etc., as in cholelithiasis, but the pain usually appears regularly, and at definite times after eating, is rarely sudden in onset and termination, does not often radiate to the right hypochondrium, and is more completely relieved by vomiting and the administration of alkalies (at least in the early stages) than that of gall-stones. Hemorrhage from the stomach or bowel is strongly indicative of ulcer, while tenderness under the right costal margin or gasping inspiration on deep palpation, enlargement of the gall-bladder, rigors, slight febrile movements, and especially jaundice are in favor of cholelithiasis. In the case of perforation of a peptic ulcer the pain is associated with marked rigidity of the abdominal muscles, the liver dulness is often obliterated, and the patient instead of tossing about in his agony, as in an attack of colic, seems to be struck motionless. The exclusion of *carcinoma of the pylorus, pancreas* or *biliary passages* may be very difficult. In carcinoma, however, the pain is rarely so acute as in cholelithiasis and, although influenced to some extent by eating, is usually more or less persistent; vomiting occurs at variable intervals, and is, as a rule, of the delayed type, and the vomitus is often copious and composed of poorly digested, foul-smelling food. Hematemesis is common. Tumor, cachexia, and ascites speak for carcinoma. Jaundice developing painlessly and insidiously with complete absence of bile from the duodenum, with distention of the gall-bladder or persistent enlargement of the liver, and with progressive loss of flesh and strength is strongly suggestive of a new growth; whereas fluctuating jaundice with contraction of the gall-bladder, the presence of bile in the duodenal contents, and the

[1] Brit. Med. Jour., May 1, 1909.

occurrence of ague-like paroxysms in which there are colicky pains, swelling of the liver, and increase in the jaundice, and in the intervals fair health, is equally suggestive of a stone in the common bile-duct. The diagnosis from *acute appendicitis* may present considerable difficulties, especially if the right lobe of the liver is elongated (Riedel's lobe) or the appendix is unusually high. As a rule, however, the location of the pain and occurrence of tenderness and swelling in the right iliac region will make a correct diagnosis possible. It must be remembered, also, that the two diseases not rarely coexist. In *chronic pancreatitis* symptoms may arise which do not differ from those of gall-stones, and in many cases both conditions are actually present. Pancreatitis may be suspected if the pain is regularly referred to the mid-epigastrium or to the left side, especially after the acute phase has subsided; if tenderness can be elicited on the left side; if there is much wasting, and if there are evidences of a diminution of pancreatic enzymes in the bowel. *Acute hemorrhagic pancreatitis* causes more profound collapse than biliary colic and is usually associated with tenderness, rigidity and distention in the epigastric region. The skin, too, is frequently cyanotic and the stools may contain blood.

At times it is difficult to distinguish between biliary and *renal colic.* Points of importance in the diagnosis are the radiation of the pain downward into the groin or external genitalia, disturbances of micturition, the presence of blood cells in the urine after an attack of pain and positive findings upon x-ray examination. *Floating kidney with attacks of pain* (Dietl's crises) has sometimes been mistaken for cholelithiasis. Among the distinguishing features, the most important are the urinary symptoms and the detection of a movable kidney on physical examination. Jaundice is rare, but it has been observed in a number of cases (Fenwick, Hale White, Moullin). The pain of the *hyperchlorhydric syndrome* is distinguished from that of biliary colic by having a direct relationship to food, and being relieved completely by alkalies and the evacuation of the stomach. Angina pectoris, lead colic, mucous colic, and the gastric crises of tabes dorsalis are not likely to be confused with biliary colic if a careful examination is made.

The intermittent hepatic fever not rarely occurring in cholelithiasis may sometimes be difficult to distinguish from *abscess of the liver.* Usually, however, the discovery of a primary source of suppuration (amebic dysentery, ulcer of the rectum, abscess elsewhere in the body), persistent enlargement of the liver, failure of the fever to subside completely between the paroxysms, and more or less serious impairment of the general health will lead to a correct diagnosis. Among other conditions causing long-continued alternating pyrexia that may bear some resemblance to intermittent hepatic fever, especially if this is unaccompanied by pain and jaundice, may be mentioned malaria, chronic infective endocarditis, visceral syphilis, pyelonephritis and Hodgkin's disease or lymphosarcoma affecting chiefly the retroperitoneal or mediastinal lymph-nodes.

**Prognosis.**—The prognosis of cholelithiasis must be guarded. Although many patients escape the serious accidents to which attention has been directed and even suffer little inconvenience, experience has shown that in the large majority of cases more or less disturbance of digestion and general impairment of health sooner or later ensue, and, moreover, that an apparently simple case may at any time take an unfavorable turn. The colic itself is rarely dangerous. In a few instances, however, death has resulted from collapse or rupture of the gall-bladder and diffuse peritonitis. Not infrequently after several attacks of colic the patient experiences no more severe pain, all of the stones having been discharged or those still in the gall-blad-

der becoming quiescent. The detection of a smooth round calculus after a first attack of colic affords some ground for hope that there may be no further trouble. In chronic obstruction of the common bile-duct the prognosis is always serious; indeed, without surgical intervention one must be prepared for a fatal issue. Occasionally, however, nature effects a spontaneous cure, the stone making its way into the duodenum through a fistula or otherwise escaping.

**Treatment.**—The medical treatment of cholelithiasis is essentially that of cholecystitis, for chronic catarrh of the gall-bladder is the chief cause of the formation of gall-stones, and when these are already present, a reactivation of the inflammatory process is mainly responsible for mobilization of the stones and the occurrence of colicky pains. Attempts to promote the solution of gall-stones or to effect their expulsion by means of drugs have met with very little, if any, success, and therefore our main reliance must be on measures which tend to allay inflammation in the biliary tract and keep the stones quiescent. These measures have already been dealt with elsewhere (see p. 505).

*Hepatic Colic.*—If the pain is severe it will be necessary to give morphin with atropin at frequent intervals. As the opium habit is readily formed in these cases it need scarcely be added that great caution should be exercised in the use of the drug. Agonizing pain often yields to a few whiffs of chloroform. In the milder but more persistent attacks a few doses of antipyrin, 5 to 7 grains (0.3–0.5 gm.) in copious draughts of hot water, may suffice. The external application of heat is very useful. Hot poultices or fomentations may be applied to the region of the liver, or if circumstances permit, the patient may be kept in a hot bath. Exceptionally, an ice-bag affords more relief than a hot application. If vomiting is excessive, carbonated water, cracked ice, small quantities of champagne, or cerium oxalate may be given. In threatened collapse diffusible stimulants are needed.

**Surgical Treatment.**—Surgical intervention is indicated—(1) when despite medical treatment attacks of colic occur so frequently and are of such severity as to cause disability or make addiction to morphin a likelihood; (2) if, as a result of chronic cholecystitis or of pericholecystic adhesions, there is intractable indigestion with non-colicky pains; (3) in persistent enlargement of the gall-bladder, even if pain and jaundice are absent; (4) in obstruction of the common bile-duct, if the symptoms persist after two, or at most three, weeks of rest, dieting and local applications of heat; and (5) if there are evidences of pancreatitis, acute or chronic. In the hands of skillful surgeons the mortality of operations on the gall-bladder in uncomplicated cases is very low, certainly less than 2 per cent. and the all-round mortality, excluding cases of malignant disease, is probably not more than 7 or 8 per cent. Complete and permanent relief may be confidently expected after operation in a very large proportion of the early cases. Cholecystectomy gives much greater prospect of permanent cure than cholecystotomy. C. H. Mayo,[1] reports that in 2,460 cases in which cholecystectomy was performed for cholecystitis with or without stones the mortality was only 1.8 per cent. Recurrence in the sense of the actual formation of new stones is rare even after cholecystotomy, subsequent disturbances usually being the result of a persisting cholecystitis, of calculi that have been overlooked during the operation, or of pericholecystic adhesions. If jaundice has been present for a long time it is advisable to administer blood serum (50 to 150 mils.) subcutaneously and calcium lactate by the mouth with the view of reducing the coagulation time of the blood and preventing capillary oozing.

[1] Surg., Gynec. and Obstet., 1920, xxx, 545.

## CARCINOMA OF THE GALL-BLADDER AND BILE-DUCTS

Carcinoma of the biliary tract may be primary or secondary. Primary carcinoma of the gall-bladder most commonly affects the fundus, and is usually due to irritation by gall-stones. Primary malignant disease of the bile-ducts may arise in any part of their course, but it most frequently begins in the common duct. Occasionally it arises in the ampulla of Vater. Gall-stones are less frequently mentioned as a cause than in carcinoma of the gall-bladder. Extension to the liver is common in both conditions. Secondary carcinoma of the gall-bladder or bile-ducts is caused by the extension of a primary growth in the liver or an adjacent organ.

**Symptoms.**—In *carcinoma of the gall-bladder* evidence of antecedent cholecystitis or cholelithiasis is usually to be had, although there is often no history of actual biliary colic. Digestive disturbances with more or less pain in the epigastric or right hypochondriac region are early manifestations. A tumor in the position of the gall-bladder, at first smooth but later nodular, firm, usually tender to touch, and sometimes movable on respiration, is present in more than two-thirds of the cases. The liver is often enlarged. Jaundice usually, but not invariably, supervenes and is likely to be persistent. Vomiting, sometimes of retained food, is common. Ascites, the result of pressure on the portal vein or of chronic peritonitis, may also occur. Symptoms due to involvement of adjacent structures are in many instances a conspicuous feature. Emaciation occurs rapidly and cachexia is often pronounced. The average duration is about 8 months.

The symptoms of *carcinoma of the larger bile-ducts* are much the same as those of carcinoma of the gall-bladder, but in the former there is less often a history of antecedent cholecystitis or cholelithiasis; jaundice, insidious in its onset and steadily progressive, is almost a constant feature; and the tumor in the position of the gall-bladder remains uniformly smooth.

**Diagnosis.**—An early diagnosis is extremely difficult. Cholelithiasis with inflammatory thickening of the gall-bladder, obstruction of the common duct by a calculus, obstructive biliary cirrhosis, and malignant disease of the liver, of the pylorus, of the pancreas, and of the transverse colon must be excluded.

**Treatment.**—When performed at an early period operation is occasionally successful. Medical treatment is, of course, merely palliative. According to Kehr,[1] a permanent cure occurred in only 2.3 per cent. of 350 operative cases. Smithies[2] reports 2 recoveries in 23 cases of primary cancer of the gall-bladder.

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## CONGENITAL IMPERMEABILITY OF THE BILE-DUCTS

This term is used to describe the comparatively rare condition in which there is either atresia of the biliary ducts or obliteration of the biliary ducts existing from birth. Anatomically, it is associated with biliary cirrhosis of the liver, and clinically it is characterized by jaundice, which is present at or appears soon after birth and is persistent, acholic stools, bile-stained urine, enlargement of the liver and spleen, hemorrhages from the navel, from the mucous membranes and into the skin, and toward the end more or less emaciation. If there is much bleeding death may occur within a few days.

[1] Berlin. klin. Woch., 1915, No. 46.
[2] Amer. Jour. Med. Sci., Jan., 1919.

otherwise the child may live from three to eight months. The nature of the condition is somewhat obscure and probably varies in different cases. Thus, the ducts may be impervious in consequence of a developmental anomaly or they may be obstructed as the result of adhesions set up by fetal peritonitis or of a prenatal cholangitis of syphilitic or non-syphilitic origin. The *diagnosis* is usually not difficult. In ordinary icterus neonatorum the stools contain bile and the pigmentation of the skin is slight and soon fades. In infective jaundice there are symptoms of general infection and often signs of inflammation about the navel. Syphilitic disease of the liver may be distinguished by a history of syphilis and other evidences of syphilis.

## DISEASES OF THE BLOOD-VESSELS OF THE LIVER

**Thrombosis of the portal vein (pylethrombosis, pylephlebitis adhesiva)** is most often found in association with cirrhosis of the liver or malignant disease of the abdominal organs, although it is not very common in either of these conditions. In cirrhosis it probably depends upon an endophlebitis set up by the increased tension in the portal vein or the absorption of toxic bodies from the intestine; in malignant disease it may be due to compression of the portal vein or to entrance into the vein of the growth itself. Septic processes (cholangitis, peptic ulcer, appendicitis, etc.) within the area of the portal system may also set up thrombosis, although they are more likely to cause suppurative pylephlebitis. Thrombophlebitis of both portal and splenic veins occurs in certain cases of splenomegaly with anemia (splenic anemia), but whether it is a primary or a secondary condition is not definitely known. Occasionally portal thrombosis results from traumatism or depends upon a primary chronic endophlebitis, which in some cases is apparently syphilitic. Pylethrombosis usually, but not invariably, leads to fatty and necrotic changes in the liver and splenic engorgement. Infarction of the liver sometimes occurs, and if the mesenteric veins are involved there may also be infarction of the small intestine. The diagnosis of portal thrombosis is rarely possible, the symptoms being strongly suggestive in some cases of hepatic cirrhosis and in others of acute intestinal obstruction. The most common features are ascites (rapidly developing), enlargement of the spleen, gastrointestinal hemorrhages, diarrhea, and abdominal pain. Enlargement of the superficial abdominal veins is sometimes observed. The condition is usually fatal, but partial recovery is occasionally effected through the establishment of a collateral circulation.

**Suppurative pylephlebitis (portal pyemia)** is usually secondary to a focus of suppuration in the gastrointestinal tract, pancreas, spleen, or liver itself. In 29 of 72 cases collected by Langdon Brown[1] the primary lesion was appendicitis. The coats of the portal vein are swollen and soft, and the vein itself, through a greater or less extent, is filled with a mass of pus and broken-down blood clot. In many cases particles are detached from the original mass and are carried into the smaller branches of the vein, producing multiple foci of suppuration, which soon involve the liver tissue itself. The symptoms are often masked by those of the primary disease. The chief features of the pylephlebitis are rigors, irregular fever, sweats, prostration, and other phenomena of the pyemic state, and certain indications of hepatic involvement, the most common being painful enlargement of the liver, jaundice and

[1] St. Barth. Hosp. Rep., 1901, xxxvii.

splenic tumefaction. Vomiting, hiccough, diarrhea and tympanites may also be present. The condition is almost always fatal, death, preceded by coma or collapse, occurring within a few weeks.

**Occlusion of the hepatic veins** is uncommon. It may be due to (1) thrombosis, (2) pressure of tumors, cysts, cicatricial adhesions, etc., (3) invasion of the veins by new-growths, (4) embolism, (5) chronic obliterative endophlebitis. Thrombosis is usually secondary to some other form of obstruction. Embolism is very rare. It may result, however, from the travelling backward of fragments of a thrombus from the inferior vena cava during a sudden reversal of the blood-flow, caused by coughing or other violent expiratory effort (retrograde embolism). In the condition known as chronic obliterative endophlebitis there is a gradual proliferation of the lining of the veins resulting in obstruction. Congenital syphilis, malformation, and perihepatitis have been suggested as etiologic factors. According to Herrick[1] there are about 30 cases on record of obstruction of the hepatic veins from thrombosis or thrombophlebitis. In many of the cases stenosis of the inferior vena cava coexisted. Cirrhosis of the liver, primary or more frequently secondary from stasis, has also been a common finding at necropsy. The clinical picture of occlusion of the hepatic veins is similar to that of portal cirrhosis of the liver, the chief features being enlargement of the liver with tenderness on pressure and ascites. Jaundice is not observed. The ascitic fluid is often blood-tinged and shows a tendency to reaccumulate rapidly after tapping. The duration of the symptoms in the reported cases ranged from a few days to several years.

**Aneurysm of the hepatic artery** is rare. In 1908 Rolland[2] collected from the literature 41 cases and since then about 14 additional ones have been reported (Weiss).[3] In the majority of cases the disease has developed after some acute infection, such as pneumonia or typhoid fever. Syphilis does not seem to be an important factor. The main trunk of the artery is affected more frequently than either of its branches. Pain simulating biliary colic, jaundice, and recurring hemorrhage from the digestive tract (leakage into the bile-ducts) are the usual symptoms. Pulsation and bruit are rarely present as the aneurysm is commonly small and deeply situated. Rupture into the peritoneum or into the biliary passages is a frequent termination. In a case reported by Kehr[4] the hepatic artery was successfully ligated.

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## CONGESTION OF THE LIVER

Two varieties of congestion of the liver are recognized—*active* and *passive*—according as the overdistention of the hepatic vessels is the consequence of increased supply of blood to, or obstructed outflow of blood from, the organ.

### ACTIVE CONGESTION

Active congestion of the liver is physiologic during digestion. Pathologically, it may be caused by overeating, especially of rich or highly seasoned food or by the excessive use of alcohol. It frequently occurs, also, as a

[1] Jour. Amer. Med. Assoc., June 26, 1920.
[2] Glasgow Med. Jour., May, 1908.
[3] Amer. Jour. Med. Sci., June, 1921.
[4] Münch. med. Woch., 1903, i, 1861.

result of malaria, typhoid fever, septicopyemia and other infections. The condition frequently observed in hot climates, which is known as "tropical liver" and which may be an acute congestion of the liver or, in severe form, a veritable acute non-suppurative hepatitis, seems to be due in some instances to immoderate eating and drinking and in others, to an infection, particularly dysentery or malaria. It is only in the infective cases of active congestion that opportunity is afforded to study the liver post-mortem. Early in these cases the organ is swollen and uniformly red, owing to over-filling of its vessels with blood. The liver-cells may show little or no alteration. Later, cloudy swelling supervenes, and as a result the organ becomes somewhat pale and on section turbid. Transitions between the two changes are frequently observed. The symptoms commonly ascribed to active congestion of the liver are those of so-called indigestion, namely, anorexia, coated tongue, epigastric discomfort, constipation, headache and malaise. In well-marked cases there may also be a sense of weight in the hepatic region and slight yellowness of the sclerae. The liver itself may be slightly enlarged and tender. The condition is not dangerous, and rarely lasts more than a few days. It has been surmised, however, that frequent recurrence may sometimes eventuate in cirrhosis. Attacks arising from errors in eating and drinking usually yield promptly to dietetic restrictions and the administration of a mercurial purge, followed by a saline—Seidlitz powder, sodium phosphate, or Rochelle salt. If there is much local discomfort stupes or a few dry cups may be applied to the hepatic region. In congestion occurring in the course of dysentery the most effective measures are rest in bed, a low diet, the application of leeches or wet cups over the liver, and the administration of Epsom salt by the mouth and of emetin hypodermically.

## PASSIVE CONGESTION

Passive congestion of the liver is due to (1) backward pressure of blood in the inferior vena cava, the result of acute or chronic failure of the heart; or, more rarely, to (2) impeded outflow of blood from the liver, the result of a local lesion that obstructs the inferior vena cava itself or the hepatic veins. Most frequently it is observed as an accompaniment of decompensated valvular disease or acute or chronic affections of the myocardium. Less commonly it occurs in the course of chronic pulmonary diseases that increase the work of the right ventricle, such as emphysema, chronic pleurisy, and cirrhosis of the lung, and occasionally it is brought about by compression of the inferior vena cava by aneurysms, tumors or enlarged lymph-nodes, or occlusion of the hepatic veins by thrombi or adhesions. The anatomical changes in the liver vary with the duration of the congestion. In the cases resulting from more or less acute heart failure the liver is uniformly enlarged and engorged with blood, but otherwise normal. In the cases depending upon long-continued back pressure of blood in the liver structural changes are always present. The organ is, as a rule, still enlarged and full of blood, and on section presents a variegated appearance, like that of a nutmeg on cross section, hence the term "nutmeg-liver."

Microscopic examination shows that the cells around the distended central vein (dark area) are shrunken, necrotic and pigmented and in part replaced by blood that has escaped from the engorged capillaries, while the cells in the outer zone of the lobule (light area) are pale and more or less fatty. These changes have been ascribed to the increased pressure of the venous blood, but recently it has been suggested that local asphyxia, interference with nutrition, and interstitial hemorrhage are the more important factors (Lambert and

Allison[1]). In the very advanced cases the liver may be small, darkly pigmented, and indurated (cirrhotic nutmeg-liver or cyanotic atrophy of the liver) owing to great loss of cells in the central zones of the lobules and to a relative, and probably an actual, increase of connective tissue.

Symptoms directly referable to the liver only become apparent when the congestion has existed for a long time or when the liver is distended beyond its capacity to act as a safety-valve to the heart. The most constant feature is enlargement of the liver, the lower margin in extreme cases sometimes reaching to or even beyond the transumbilical line. The degree of enlargement may vary considerably within a short time, decreasing or increasing according as the patient's circulatory condition becomes better or worse. There is often a feeling of weight in the right hypochondrium, and if the capsule is tightly stretched there may be actual pain and tenderness. Exceptionally an expansile systolic pulsation is observed. Jaundice, usually slight and apparently due to secondary catarrh of the bile-ducts, is common, and not rarely produces in combination with the cyanosis a characteristic purplish yellow complexion. Ascites is present in many cases. Usually it is proportionate to the edema of which it is a part, but occasionally, in consequence of secondary cirrhotic changes in the liver or of chronic peritonitis, it is disproportionately large and requires repeated tappings. Dyspnea, digestive disturbances, and oliguria are also commonly present, but these symptoms are more closely related to the primary cardiac or pulmonary disease than to the hepatic congestion.

The treatment is chiefly that of the primary disease. Rest in bed and a diet of light easily digestible food are important measures. The bowels should be kept freely open by salines or mineral waters containing them and occasional courses of calomel or blue mass. The application of a few wet cups or leeches over the liver is often efficacious, and if there is much cyanosis benefit may be derived from venesection to the extent of from 10 to 20 ounces.

## ABSCESS OF THE LIVER

**Etiology.**—Abscess of the liver is almost always due to infection with ordinary pyogenic organisms or the ameba of dysentery. In rare instances, however, typhoid bacilli, the colon bacillus, pneumococci, or the Actinomyces bovis may be the inciting agent.

The bacteria may reach the liver (a) by direct extension of disease from adjacent organs, (b) by direct implantation (trauma), (c) through the portal vein, (d) through the hepatic artery, (e) through the biliary passages, or very rarely (f) through the hepatic veins (retrograde embolism). In the large majority of cases the infection atrium is in the area of the portal vein, the abscess arising as a complication of ulcerative disease of the stomach or intestines, acute appendicitis, salpingitis, or pelvic cellulitis. The most common abscess is that resulting from amebic dysentery, and which has been known as tropical abscess, because it is observed chiefly in persons who live or have lived in hot climates. Over indulgence in food and drink seems to favor its occurrence, and for this reason, perhaps, it is more prevalent among Europeans and Americans in the tropics than among the more abstemious natives. Cases are sometimes observed in which no history of dysentery is obtainable, but even in these cases an amebic infection of the bowel probably existed at one time, although it may have been latent or productive of no

[1] Johns Hopkins Hosp. Bull., 1916, xxvii, 350.

disturbance other than a transient diarrhea which the patient soon forgot. The route by which the amebæ reach the liver is not definitely known, but it is supposed to be the portal vein.

Apart from infection in organs tributary to the portal vein the most common causes of hepatic suppuration are traumatism, general pyemic processes, including malignant endocarditis, and infection of the biliary passages, especially suppurative cholangitis. Traumatism may be effective with or without a penetrating wound. In the absence of a wound it acts by creating a *locus minoris resistentia*. In general pyemia the infection is embolic and usually by way of the hepatic artery. Hydatid cysts sometimes become infected and suppurate, and occasionally the presence of round worms or flukes in the intrahepatic bile-ducts gives rise to an abscess.

**Morbid Anatomy.**—Amebic abscesses are usually solitary and situated in the right lobe. The average of various post-mortem statistics indicates that two are present in about 10 per cent. of the cases and more than two in about 20 per cent. of the cases, but as these statistics deal chiefly with incurable abscesses, they show, of course, an excess of multiple cases. Single abscesses sometimes reach enormous proportions. The material within the absecss may be creamy and yellow like ordinary pus, but more commonly it is viscid and has a reddish or brownish hue from the admixture of blood and broken-down liver tissue, the process in pure amebic infections being one of liquefaction necrosis rather than of inflammation. Microscopic examination of the fluid shows granular detritus and red blood-cells, but relatively few leucocytes. In many cases the amebæ are confined to the walls of the abscess and are not found in its contents. Not rarely two or three days elapse after an abscess has been opened before amebæ appear in the escaping pus. The ordinary pyogenic microörganisms are sometimes present, with the amebæ. The liver tissue around the area of necrosis is the seat of cloudy swelling and reactionary inflammation. Traumatic abscesses are also usually solitary and, as a rule, in the right lobe. The contents consist of ordinary pus, which in most cases shows numerous bacteria. Metastatic abscesses and those secondary to suppurative cholangitis are almost always multiple and are usually of small size. In some instances of abdominal infection, however, the abscess is solitary and unaccompanied by pylephlebitis.

Rupture of large abscesses is comparatively frequent, the perforation taking place into the lung, the pleura, the pericardium, the abdominal cavity, the stomach or intestines, or externally. In more than one-third of the cases that rupture spontaneously the lung is penetrated and the pus is discharged through a bronchus. In a few cases rupture has occurred into the hepatic veins or the inferior vena cava. Single small abscesses sometimes become permanently quiescent through inspissation of the pus and encapsulation.

**Symptoms.**—A solitary abscess of the liver, even if large, may remain latent and only be discovered at necropsy, or it may produce indefinite symptoms and not be suspected until spontaneous rupture occurs. In most cases, however, the clinical picture is sufficiently characteristic to lead to a correct diagnosis. The onset is sometimes sudden and marked by a chill, but usually it is insidious, the patient for weeks or even months complaining of failing appetite, disturbed digestion, weakness and emaciation. Localized pain and symptoms of general septicemia, such as fever, sweats, chills and polymorphonuclear leucocytosis, are commonly present. The pain varies greatly in intensity and is frequently referred to the right shoulder or scapular region or to the right clavicle. The patient is, as a rule, most comfortable when lying on the back or on the right side. The fever sometimes

reaches 104° or even 105° F., and may be intermittent or extremely irregular. Occasionally, especially in the more chronic cases, the temperature is normal throughout. Jaundice occurs in less than one-fourth of the cases and is usually slight. If marked it may be due to pressure upon the common bile-duct or to some concomitant condition, such as cholelithiasis. Nausea and vomiting may occur and diarrhea is not uncommon. Intestinal hemorrhage, the result of interference with the portal circulation or of ulceration of an hepatic vessel and discharge of blood into the bile-ducts, is an occasional symptom and may be the immediate cause of death. Dry cough due to irritation of the diaphragmatic pleura is often present and is especially marked when perforation into the lung is imminent.

Even in the absence of jaundice, the complexion is often sallow or muddy. There is commonly some degree of secondary anemia and polymorphonuclear leucocytosis is usually, but not always, present. Enlargement of the liver occurs in the large majority of cases. It is rarely uniform, and as the dome of the organ is the favorite site of the abscess the enlargement is often more upward than downward. Distinct bulging corresponding to the position of the liver is not infrequently observed. In large abscesses the dulness may extend upward as far as the second rib and downward as far as the crest of the ileum. Tenderness in the hepatic region is usually present and in many cases more or less rigidity of the right rectus is observed. In very rare instances palpation reveals a sense of fluctuation. The superficial abdominal veins are sometimes distended and occasionally there is localized edema of the abdominal wall. Friction rubs, due to perihepatitis or to pleurisy, are fairly common, and so too are signs of compression at the base of the right lung. Roentgenographic examination may aid in determining the location and the size of the abscess. Enlargement of the spleen is sometimes observed, but ascites is rare. Multiple abscesses of the liver often escape recognition as the symptoms are usually more or less obscured by those of the primary disease or general septicopyemia. They should be suspected in conditions likely to cause hepatic suppuration if there is pain in the region of the liver, with enlargement of the organ and local tenderness, and particularly if jaundice is also present.

**Course and Termination.**—Solitary abscesses if not operated upon may rupture or remain intact. Rupture occurs in more than 25 per cent. of the cases and most frequently is into the lung, with the production of a pulmonary abscess and the discharge of the pus through a bronchus. In this event the expectoration is often chocolate-colored and may contain shreds of hepatic tissue and amebæ. Hepato-pulmonary abscess not rarely terminates favorably, but it may prove fatal through exhaustion, hemoptysis or secondary cerebral abscess. Rupture into the pleura and into the intestinal, tract are sometimes followed by recovery, but rupture into the peritoneum, unless it occurs slowly with the formation of a subphrenic abscess, is nearly always fatal. Hepatic abscesses that remain intact almost always lead to death, this being due, as a rule, to septicopyemia. Occasionally spontaneous cure is effected through the caseation and encapsulation of the pus. The duration of solitary abscesses varies from a few weeks in the acute forms to several months or even years in the chronic forms. In cases treated expectantly the mortality may be as high as 90 per cent., while in cases treated by early evacuation of the pus the mortality may be only 25 or 30 per cent. Although relapse is extremely common in intestinal amebiasis, recurrence in amebic abscess of the liver is comparatively rare. Multiple abscesses are almost invariably fatal within a few days or weeks.

**Diagnosis.**—The diagnosis of suppurative hepatitis is often attended with

difficulty. It must rest upon a history of dysentery or other etiologic factor, upon the development of the septicemic state, and upon evidence that the liver is involved. When there are reasonable grounds for suspecting hepatic abscess, especially the amebic form, exploratory puncture, under anesthesia, with the needle of an aspirating syringe may become necessary to establish the diagnosis, although the procedure is not entirely free from the risk of hemorrhage or peritonitis. The conditions most likely to be mistaken for hepatic abscess are suppurative cholangitis, intermittent hepatic fever, suppurative pylephlebitis, and syphilitic disease of the liver. In *suppurative cholangitis* jaundice is common, appears earlier, and is more pronounced than in abscess. A history of cholelithiasis is also in favor of cholangitis. In *intermittent hepatic fever* there are periodic attacks of fever and chill, separated by longer or shorter intervals of apyrexia and fair health. Pain, leucocytosis, and hepatic enlargement are rarely continuous, as in abscess; jaundice is commonly present and is intensified during the febrile attacks; and the history usually points to cholelithiasis. It is often impossible to distinguish between a solitary abscess of the liver and *pylephlebitis with multiple hepatic abscesses*. A history of abdominal suppuration rather than of dysentery, rapid emaciation and prostration, pronounced enlargement of the spleen, and the early occurrence of marked jaundice are in favor of pylephlebitis. *Syphilis of the liver* accompanied by fever and considerable enlargement of the organ may readily be mistaken for hepatic abscess. A history of syphilitic infection, other evidences of syphilis, especially a positive Wassermann reaction, striking irregularity of the organ, ascites, and a relatively marked enlargement of the left lobe as compared with the right should suggest the possibility of syphilis and a trial of the therapeutic test.

**Treatment.**—The treatment of amebic abscesses of the liver is both medical and surgical; that of other solitary abscesses is almost exclusively surgical. The treatment of multiple pyemic abscesses is that of general septicopyemia and is chiefly palliative. By intramuscular injections of emetin hydrochlorid (see p. 209) it is apparently possible not only to cure amebic dysentery giving rise to liver abscess but also to check abscess formation itself in its earliest stages. Once a liver abscess has been definitely formed, however, the sooner the pus is evacuated the better. Many East Indian surgeons of large experience prefer aspiration to incision and drainage, especially in the very acute forms, but whether one or other procedure is adopted, the use of emetin as an adjuvant is always advisable. Other therapeutic measures include absolute rest, a light diet, cold or warm applications over the hepatic region, and the administration of mild laxatives. During convalescence nourishing food, fresh air, and tonics are necessary. On account of the possibility of recurrence it is advisable for the patient to reside in a temperate climate for at least two years after operation. In single non-amebic abscesses the only recognized method of treatment is free opening and drainage.

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## CIRRHOSIS OF THE LIVER

The term cirrhosis is at present generally applied to any morbid change in the liver in which hyperplasia of the fixed connective tissue and atrophy of the specialized cellular elements are a conspicuous feature, although originally it was used by Laennec to describe the yellow color of the nodules ("hobnails") appearing on the surface of the organ in a common form of fibrosis.

An excess of fibrous tissue occurs in the liver in a variety of conditions, but in only two are the morbid changes and functional disturbances sufficiently distinctive to be regarded as definite entities. One of these two conditions is known as *portal or atrophic cirrhosis*. It is usually caused by alcoholism and is characterized by diminution or moderate increase in the size of the liver, by symptoms of portal obstruction (ascites, hematemesis, etc.), and, in the majority of cases, by absence of jaundice. The second of these two diseases is known as *biliary cirrhosis*. Two types are usually recognized. In one, Hanot's type, the etiology is obscure, although an infectious origin is suspected; in the other, obstructive biliary cirrhosis, the causative factor is gross obstruction of the bile-ducts. In both of these types the liver is persistently enlarged, jaundice is constantly present, but ascites and other symptoms of portal obstruction are usually absent.

Among other diseases of the liver in which fibrosis occurs are the following: (1) Chronic perihepatitis (capsular cirrhosis.) Not rarely in this disease fibrous bands project from the thickened capsule into the substance of the liver and the latter shows varying degrees of atrophy as a result of compression. (2) Cyanotic atrophy. In long-standing passive congestion of the liver, the result of cardiac disease (cardiac liver), there is always more or less fibrosis about the central veins in consequence of atrophy of the liver cells. The supporting reticulum is increased not only relatively but absolutely (replacement fibrosis). (3) Syphilis of the liver. With the exception of the acute parenchymatous hepatitis with jaundice occasionally observed during the secondary manifestations, the hepatic changes due to acquired syphilis almost always include a proliferation of connective tissue. In the progressive stage there is usually a combination of gummata, large or miliary, with fibrosis, and after the process has run its course there are dense cicatrices which send out radiating processes into the liver substance, dividing it into a number of irregular masses or lobes (hepar lobatum). In inherited syphilis there may also be gummata with fibrosis, but the more common change is a separation of liver cells by small embryonic cells, which in the course of time may develop into fibrous tissue producing a diffuse pericellular or monocellular type of cirrhosis, quite characteristic of syphilis. Whether syphilis ever produces directly ordinary multilobular cirrhosis of the liver of the Laennec type is somewhat doubtful, although it seems to favor its occurrence. (4) Various focal lesions of the liver. Under this head are included the circumscribed fibrosis occurring around cysts, parasites, tubercles, etc., and the patches of fibrosis, usually small and widely disseminated, that replace foci of necrosis the result of acute infections or intoxications. If the cause of the necrosis is a transient one, such as a single attack of some acute infection, the fibrosis may be stationary and unassociated with any symptoms. On the other hand, if the underlying infection or intoxication causing the necrosis is persistent the fibrosis may become a part of a progressive process of destruction and repair and finally develop into a veritable cirrhosis.

## PORTAL CIRRHOSIS

**(Atrophic Cirrhosis; Multilobular Cirrhosis; Laennec's Cirrhosis; Hobnailed Liver)**

**Etiology.**—Although occasionally observed in children, portal cirrhosis is essentially a disease of adult life. It is usually first recognized after the age of 35, and the average age at death is about 50. It is three or four times more common in men than in women. The disease is undoubtedly due to the action of irritants brought to the liver by the bloodvessels, especially

the portal vein. In the large majority of cases it follows the excessive use of alcohol, particularly in the form of spirits (whiskey, gin, brandy), although malt liquors are not without influence. However, as cirrhosis occurs in only a small proportion of drunkards (4 or 5 per cent.), as it sometimes arises when a history of alcoholism is certainly absent, and as it cannot readily be produced in lower animals by the administration of alcohol alone there is good reason for believing that the part played by alcohol in the production of the disease is an indirect rather than a direct one. It has been suggested that alcohol lessens the resistance of the liver and also sets up a gastro-intestinal catarrh, and that in consequence of the latter, poisonous substances from abnormal fermentation or toxins from intestinal auto-infection are set free, which being conveyed to the liver bring about the cirrhotic change. Experimental studies have shown that toxic substances having a special affinity for the liver when associated with mild bacterial infection are more prone to produce cirrhosis than either the poisons or the bacteria when acting alone (Ramond, Opie). It is likely that in some instances other irritants, ingested preformed with the food or manufactured in the intestinal canal as a result of disordered digestion, may play the part usually taken by alcohol in the genesis of the disease. Experimentally, cirrhosis has been produced by the administration of fatty acids (Hanot and Boix), phenol and indol (Metchnikoff), chloroform (Nothnagel, Mertens, Opie), ricin (Flexner), phosphorus (Wegner, Aufrecht), hemolytic immune sera (Pearce) and various proteins in animals previously sensitized to them (Longcope).

Italian pathologists incline to the view that toxins arising in the spleen may induce hepatic cirrhosis (Banti's disease), but the question is by no means settled. The cirrhosis occurring among Mohammedans and Brahmins, who avoid alcohol, has been ascribed to the free use of spices and other stimulating articles of food. Potain[1] and Lafitte[2] have cited a few human cases of the disease in chronic lead poisoning. Acute infections are sometimes followed by cirrhosis, but the exact relationship of these processes to the changes in the liver is somewhat obscure. Kelsch and Kiener[3] describe a malarial cirrhosis, but this condition has not been observed in America. Syphilis, especially the inherited form, seems to favor the occurrence of true portal cirrhosis, probably by lessening the resisting power of the liver. It is doubtful, however, whether syphilis ever directly produces the disease. The tuberculous lesions often found in association with cirrhosis of the liver are usually secondary, but the researches of Hanot and Gilbert,[4] Stoerk[5] and others suggest that mild tuberculous infections reaching the liver from the bowel may in exceptional cases produce cirrhotic changes instead of tubercles. Cirrhosis of the liver is not infrequent in the later stages of kala-azar.

**Morbid Anatomy.**—Pathologically the disease is characterized by an excess of fibroid connective tissue, a variable degree of atrophy or destruction of the hepatic parenchyma, and a regenerative proliferation of some of the surviving liver cells. The liver varies in size in different cases and also at different times in the same case. At autopsy it is usually smaller than normal and in extreme cases may weigh less than 1000 grams, but not uncommonly it is increased in size weighing as much as 5000 grams or more. Enlargement of the organ may depend upon associated fatty changes, pronounced hyperplasia of the liver cells, or vascular engorgement. The surface of the organ presents numerous fine or coarse nodules ("hobnail" liver)

[1] Sem. Méd., 1888, viii.
[2] Thèse de Paris, 1892.
[3] Archiv. de physiol. norm. et path., 1878, 1879.
[4] Soc. de biol., Jan. 30, 1892.
[5] Wien. klin. Woch., 1907, xx.

ranging in size from that of a millet seed to that of a large pea and varying in color from light yellow to greenish-yellow or brown. Large livers rarely present coarse nodules. Between the projections the tissue is of a grayish color and somewhat translucent. The projections represent original lobules or lobular masses of newly formed liver cells that have been pressed outward by contracting bands of fibrous tissue. The capsule of the liver is sometimes thickened and not rarely it is adherent to the diaphragm. The organ is tough and in extreme cases it may creak under the knife. The cut surface presents a grayish-white network of fibrous connective tissue, enclosing in its meshes areas of yellowish or brownish liver substance, ranging in size from that of a pin-point to others 1 cm. or more in diameter.

Microscopically, the most conspicuous feature is the great increase of fibrous tissue. This apparently takes origin in the periportal spaces, where it is most abundant, and is irregularly distributed. Although it shows a special tendency to form compartments enclosing several contiguous lobules (multi-lobular cirrhosis), it not rarely surrounds single lobules, and in advanced cases, it may even penetrate the lobules themselves to a greater or less extent and separate individual liver cells. When the process is still active the connective tissue is abundantly infiltrated with small round cells, but when it is advanced and stationary it is nearly acellular and cicatricial. The fibrous bands are often traversed by columns of cuboidal cells in a state of active growth, suggesting new bile-ducts. The origin of these structures, so-called pseudobiliary canaliculi, is still a matter of doubt, although it is generally believed that they represent an attempt at compensatory hyperplasia and are derived in part from preëxisting bile capillaries and in part from the liver cells themselves. In some forms of cirrhosis (pigmentary cirrhosis) both the fibrous tissue and the hepatic cells are studded with brownish opaque granules of pigment.

Many of the liver cells show marked retrogressive changes; some are atrophic, others are fatty On the other hand, evidences of compensatory regeneration are not wanting. In addition to the newly formed pseudo-bile ducts already described, large clear cells are observed, which from their brilliant staining and multiple nuclei must be regarded as the product of an active proliferation of the relatively intact parenchyma. These newly formed cells are usually found at the margin of a lobule, but sometimes in advanced cases they make up an entire lobule, many of the "hobnails" observed macroscopically in cirrhosis consisting of such hyperplastic (so-called adenomatous) masses. In many of the lobules the cells are pressed out of the normal radial order and the central vein is absent or is eccentrically situated.

The spleen is moderately enlarged and frequently is adherent to contiguous structures. The gastro-intestinal tract shows evidences of chronic catarrhal inflammation and also many dilated and tortuous veins, which rupturing, sometimes give rise to fatal hemorrhages. Fibrosis of the pancreas is observed in a fairly large proportion of cases. Except in the pigmented form (bronzed diabetes), however, the islands of Langerhans are not often affected. The kidneys frequently reveal interstitial changes. Chronic peritonitis, simple or tuberculous, is also a common finding.

**Nature and Effects.**—The view formerly held that cirrhosis of the liver is a primary interstitial hepatitis is no longer tenable. Recent studies indicate that the cause of the disease, whatever it may be, brings about degeneration and destruction of certain liver cells, especially at the periphery of the lobule, and that this primary damage to the parenchyma is followed by an increase in the connective tissue and also by regenerative proliferation on the part of

of the surviving living cells, leading to partial restoration of the affected lobule. According to this view the excess of connective tissue is largely a replacement fibrosis, similar to that occurring in the fibroid heart and the red granular kidney, although it is generally conceded that some of the excess may be due to an inflammatory reaction excited by the same irritant that has caused destruction of the parenchymatous cells. Contraction of the fibroid connective tissue compromises still further the nutrition of the liver cells, both old and new, and also leads to obstruction and obliteration of some of the interlobular and intralobular branches of the portal vein. The evil consequences of obstruction to the passage of blood through the liver are for a time averted by the establishment of freer communications between the tributaries of the portal vein and the general systemic veins.[1] When the collateral circulation becomes inadequate symptoms of portal stasis (ascites, hematemasis, etc.) make their appearance, and when the degenerative changes affecting the parenchyma predominate over the regenerative changes, and the intact cells are no longer competent to maintain the metabolic functions of the organ in approximate equilibrium, evidences of hepatic insufficiency supervene, usually in the form of a general toxemia, caused, it is supposed by failure of the liver cells to arrest poisons manufactured in the alimentary canal.

The splenic enlargement probably depends partly upon portal obstruction and partly upon some general toxemia, such as that which has caused the cirrhosis, or one secondary to hepatic insufficiency. The changes in the pancreas are probably due to the same cause as the hepatic cirrhosis; indeed, in some instances the latter appears to be a part of a general disorder affecting alike the liver, pancreas, spleen and kidneys.

**Symptoms.**—Cirrhosis of the liver may remain latent for years, and is often found at autopsy when its existence has been unsuspected during life. The earliest symptoms usually arise from digestive disturbance and are scarcely distinguishable from those that often result from alcoholism itself. Many patients complain of epigastric discomfort, flatulence, irregular action of bowels, and occasional attacks of vomiting. In some cases transitory attacks of dull pain in the right hypochondrium with slight jaundice and fever also occur. In alcoholic subjects the persistence of these symptoms, especially if associated with enlargement of the liver, should excite a suspicion that cirrhosis is present. As the disease advances obstruction to the portal circulation ensues and frequently leads to increasing disturbance of the digestive functions, hemorrhages from the stomach or bowel, enlargement of the spleen, distention of the veins in the abdominal wall, and ascites.

Hematemesis occurs in more than 25 per cent. of all cases in which death is directly due to cirrhosis.

It is frequently an early symptom and in many cases it is the first evidence of serious disease. Although usually severe, it is not often the immediate cause of death. Occasionally, however, the first hemorrhage proves fatal.[2] The bleeding usually results from the rupture of varicose veins at the lower end of the esophagus, but it may be a capillary oozing or come from erosions

[1] More or less free intercommunication between the portal and systemic veins is secured by dilatation of (1) the retroperitoneal veins (Retzius), which unite the portal system with the internal mammary, lower intercostal, and lumbar veins; (2) the veins in the suspensory and round ligaments of the liver (Sappey) which unite the portal with the epigastric, internal mammary, and diaphragmatic veins; (3) anastomoses between the gastric and esophageal veins; and (4) anastomoses between the superior hemorrhoidal (inferior mesenteric vein) and the middle and inferior hemorrhoidal veins.

[2] See "Sixty Cases of Fatal Gastro-intestinal Hemorrhage due to Cirrhosis of Liver. Preble, Amer. Jour. Med. Sci., Mar., 1900.

in the gastric mucous membrane. Melena frequently accompanies or follows the hematemesis, some blood escaping from the stomach into the duodenum. Less frequently the intestine itself is the source of melena. Hemorrhages from other sources, especially the nose, and into the skin and mucous membranes, are not uncommon, and may depend upon changes in the vessels, general toxemia or some concomitant condition. Enlargement of the spleen, usually moderate, is observed in the large majority of cases, and may be out of proportion to the degree of obstruction in the portal circulation.

Ascites (see p. 561) occurs in from 50 to 60 per cent. of all cases, and is much more common with small than with large cirrhotic livers. It is usually a late event, although it may be the first obtrusive symptom of the disease. It is mainly due to increased pressure in the portal vein, but complicating perihepatitis or widespread chronic peritonitis, cardiac failure, toxemia arising from hepatic insufficiency, or, more rarely, thrombosis of the portal vein may at times also play an important part in its production. When due to simple venous stasis the ascitic fluid is clear, yellowish or greenish-yellow, and alkaline. Its specific gravity is usually between 1008 and 1015, it contains from 0.5 to 2.5 per cent. of protein, and microscopically it shows only a few endothelial cells and blood corpuscles. In cirrhosis complicated by chronic peritonitis the fluid has a higher specific gravity, contains more protein, and is often turbid. Occasionally the ascitic fluid is hemorrhagic or chyliform. Edema of the lower extremities is frequent in the later stages of the disease, and is usually to be ascribed to pressure of the abdominal contents upon the inferior cava. Occasionally, however, it precedes the ascites, and in this event it may be due to cardiac weakness, alcoholic neuritis, or the action of poisons having a lymphagogue action (Hale White). Hydrothorax, commonly right-sided, may also accompany the ascites. The superficial veins over the distended abdomen are, as a rule, plainly visible, and exceptionally one sees a collection of varices around the navel, constituting the so-called "caput Medusæ." A venous hum may sometimes be heard in the epigastrium, in the region of the navel or in Traube's space, and probably depends upon the passage of blood from small veins to larger varicose ones.

At first the liver usually is enlarged, and in many cases it remains so throughout, its hard edge and even its granular or nodular surface being readily recognized by the hand. In most cases, however, the organ is ultimately reduced in size and not easily accessible to palpation. Even percussion often fails to give an accurate idea of the size of the organ, owing to the presence of ascites, meteorism, or pulmonary emphysema. Sometimes at the commencement of the disease and for brief periods during its progress there may be local discomfort and tenderness, due to vascular engorgement of the organ or attacks of perihepatitis. Jaundice supervenes in only a minority of cases (20 to 30 per cent.) It is slight, as a rule, and probably in most cases dependent upon catarrh of the intrahepatic bile-ducts. Decided jaundice occasionally develops in the advanced stages, in consequence of a superimposed acute atrophy, and is then, of course, ominous. The disease is often afebrile throughout its course, but paroxysms of fever (100°–102° F.) are not uncommon and may be due to attacks of perihepatitis, intercurrent infections, or possibly acute phases of the cirrhotic process itself. The occurrence of continued fever late in the disease usually indicates secondary infection, and most frequently tuberculosis.

Late in the course of cirrhosis there are marked evidences of disturbed nutrition. The complexion is of a sallow or brownish hue, the face is thin and

drawn, the skin is dry and harsh, and frequently the seat of small stellate varices or capillary nevi, and the limbs and trunk are wasted, being in sharp contrast to the distended abdomen. The urine is commonly reduced in quantity and concentrated. It sometimes contains a small amount of albumin, but rarely, except in pigmented cirrhosis (bronzed diabetes), any sugar. The determination of the pathologic urobilin in the urine, of the blood urea and of the tolerance to carbohydrates (levulose and galactose) has not afforded much aid in diagnosis, because in the majority of cases a sufficient amount of functionally competent liver tissue remains to carry on the work of the organ with considerable efficiency.

Toxic phenomena are usually of late occurrence and are often terminal, but they may appear at almost any stage of the disease. The more severe toxic symptoms resemble those of uremia and generally comprise delirium, stupor and coma. Less frequently convulsions and paralyses also occur. Occasionally fatal coma quickly supervenes in cases in which ascites, hemorrhages or other obstructive symptoms have never appeared.

**Portal Cirrhosis in Children.**—Hepatic cirrhosis is rare in children. In 1911 Woolley,[1] collected 90 cases under 21, the average age being 11 years. A family form has been reported by Rolleston,[2] Bramwell,[3] and others. The symptoms are much the same as those observed in adults, but the enlargement of the liver and spleen is usually more pronounced, hematemesis is less common, and jaundice and febrile paroxysms occur somewhat more frequently. A diagnosis of tuberculous peritonitis is likely to be made.

In a small group of cases the hepatic changes are associated with degeneration of the lenticular nuclei of the brain, producing the disease known as *progressive lenticular degeneration* (see p. 973), which is characterized by tremors, dysarthria, dysphagia, spasticity, contractures, various psychic disturbances, and progressive weakness and emaciation.

**Cirrhosis of Hemochromatosis (Pigmentary Cirrhosis, Bronzed Diabetes).** This rare disease occurs usually between the ages of 30 and 60 and has been observed chiefly in males. The cardinal features are (1) pigmentation of the viscera, especially the liver and pancreas, and usually also of the skin; (2) cirrhosis of the liver, almost always of the portal (multilobular) type; and in the late stages (3) diabetes mellitus, usually severe, and due to fibrotic changes in the pancreas. Occasionally diabetes fails to develop. Although life may be prolonged for many years, death is rarely deferred for more than one year after the onset of the diabetes. Coma is, as a rule, the immediate cause of the fatal issue. The etiology of the disease is obscure, but the view is generally held that some toxic substance, probably alcohol in many cases, causes disturbances in metabolism which bring about both the fibrotic changes in the liver and pancreas and the deposition of iron-containing pigment in the tissues. Whether the pigmentation depends upon increased blood destruction or inability to get rid of iron by the usual channels is still a disputed question, but the absence of pronounced anemia in bronzed diabetes is opposed to the view that it is due to excessive hemolysis. Blanton and Healy[4] analyze the 81 cases of hemochromatosis recorded in the literature and report 4 additional ones.

**Complications.**—Tuberculosis is a postmortem finding in more than 20 per cent. of all cases of cirrhosis, and in at least 10 per cent. it is the immediate cause of death. The disease shows a special predilection for the lungs and

[1] Quoted by Rolleston, Brit. Med. Jour., Sept. 2, 1911.
[2] *Ibid.*
[3] Edinburgh Med. Jour., Aug., 1916.
[4] Archives Int. Med., April 15, 1921.

peritoneum, and is frequently overlooked during life. Other infections, notably pneumonia, erysipelas, and endocarditis, are also common. Chronic nephritis is present in a considerable proportion of cases. Peripheral neuritis sometimes develops and may be the result of alcoholism or, occurring late in the disease, of the toxemia arising from hepatic inadequacy. Thrombosis of the portal vein is not an uncommon complication. Occasionally primary carcinoma of the liver coexists with cirrhosis (see p. 536).

**Diagnosis.**—The diagnosis of cirrhosis in the early stages is not always possible. However, the occurrence of persistent indigestion with enlargement of the liver or the recurrence of transitory attacks of pain in the hepatic region with slight fever and jaundice in alcoholic subjects should always arouse suspicion. Later when hematemesis, ascites, etc. have occurred the diagnosis becomes extremely probable. When there is hematemesis but no ascites it is necessary to exclude *peptic ulcer*. Pain occurring paroxysmally and related to the ingestion of food, repeated hemorrhages, and circumscribed tenderness are in favor of ulcer, whereas a history of alcoholism, and enlargement of the liver and spleen are in favor of cirrhosis. Profuse hemorrhage without other obvious symptoms is more characteristic of cirrhosis than of ulcer. In some cases the x-ray offers the only means of making the differentiation. When ascites has developed one must exclude cystic tumors of the abdominal organs and other conditions causing peritoneal effusion. Of cystic tumors, the *ovarian cystadenoma* is the one that most often comes into question. The points of distinction between the two conditions are considered on p. 563.

The ascites due to *cardiac or renal disease* is not likely to be mistaken for that resulting from cirrhosis if the condition of the heart and urine is carefully studied. The differentiation of *thrombosis of the portal vein* from cirrhosis of the liver is rarely possible; indeed, the two conditions are often associated. Thrombosis may be suspected if ascites develops suddenly with either acute abdominal pain or with melena. Ascites with distention of the abdominal veins and enlargement of the spleen is also observed in *primary obliterating endophlebitis of the hepatic veins*, but this condition is very rare and a positive diagnosis has never been made *intra vitam*. More important is the distinction between cirrhosis and chronic peritonitis. In *tuberculous peritonitis* there is frequently evidence of tuberculosis elsewhere. A history of antecedent pleurisy is suggestive. Persistent abdominal pain and tenderness, induration around the umbilicus, enlargement of the inguinal lymph-nodes and a positive tuberculin test are in favor of tuberculous peritonitis. On the other hand, gastro-intestinal hemorrhages, distention of the subcutaneous abdominal veins, tumefaction of the spleen and the occurrence of jaundice are in favor of cirrhosis. The detection of irregular masses within the abdominal cavity points strongly to tuberculosis. Again, the ascitic fluid of tuberculous peritonitis in comparison with that of cirrhosis is usually of higher specific gravity (above 1015), is richer in protein (more than 2.5 per cent.), microscopically shows more lymphocytes than endothelial cells, and when injected into guinea pigs gives rise to tuberculosis. In children ascites is much more suggestive of tuberculous peritonitis than of cirrhosis. The combination of cirrhosis and tuberculous peritonitis, by no means uncommon, can be recognized with certainty only when definite indications of both conditions are present. In *chronic hyperplastic peritonitis* (see p. 558) the etiologic factors of cirrhosis are absent, the course is slow, the ascites often remains stationary for long periods, and returns again and again after tapping, and signs of portal obstruction, other than ascites, are usually lacking. Cases in which the patient has survived numerous tappings are usually

examples of chronic peritonitis. For the diagnosis between cirrhosis and *malignant disease of the peritoneum*, see p. 560.

When enlargement of the liver is the obtrusive feature one must exclude such conditions as carcinoma, biliary cirrhosis of the Hanot type, Banti's disease and syphilis. The resemblance to *carcinoma* may be very close. A history of chronic alcoholism, a smooth or "granular" enlargement of the liver, and enlargement of the spleen point to cirrhosis; whereas, large umbilicated nodules on the surface of the liver, marked pain and tenderness, and enlargement of the gall-bladder are in favor of carcinoma. Jaundice is more frequent and, as a rule, more intense in carcinoma than in cirrhosis. Enlarged lymph-nodes above the clavicle and a primary growth in some other structure are direct evidence in favor of cancer. *Biliary cirrhosis of the Hanot type* usually occurs in young and non-alcoholic subjects. It gives rise to marked and persistent jaundice, but is seldom productive of ascites, hematemesis or dilatation of the subcutaneous veins. In *Banti's disease* alcoholism is not an etiologic factor, the splenic enlargement, which is often enormous, usually precedes the occurrence of any symptoms referable to the liver, and examination of the blood commonly reveals pronounced anemia of the secondary type with leucopenia. It must be admitted, however, that cases are not rarely seen which appear to be transitional between atrophic cirrhosis of the liver and Banti's disease. *Syphilitic disease of the liver* frequently presents great difficulty in the differential diagnosis. The history of syphilitic infection, the presence of other signs of syphilis, and marked unevenness of the hepatic contour (especially of the right-lobe) may clear up the diagnosis. In any case if the Wassermann reaction is positive vigorous specific treatment should be instituted.

**Course and Prognosis.**—Owing to the insidious onset of cirrhosis the duration of the disease cannot easily be determined, but actual recovery never occurs and the end usually comes within two or three years after the diagnosis is made clear. However, even when ascites has developed and the patient has been tapped, or copious hemorrhage has occurred the morbid process may become latent and remain so for a long period. Apart from ascites and recurrent hematemesis, the most unfavorable features are rapid emaciation, edema of the legs, drowsiness or delirium, persistent pyrexia, and general hemorrhages. Death is usually due to a general toxemic condition, increasing malnutrition, or intercurrent disease, such as pneumonia, erysipelas or tuberculosis. Occasionally it is the result of hemorrhage. In some instances the end is hastened by the development of an uncontrollable diarrhea.

**Treatment.**—In the hope that something may be done to arrest the progress of the disease, alcohol, all stimulating and highly seasoned foods, and all foods likely to increase the digestive disturbances, such as articles rich in fat or sugar, should be prohibited. Eggs, tender meat, and well-cooked vegetables and cereals may usually be allowed, but in some cases an exclusive milk diet for the first three or four weeks is advisable. Often as much depends upon temperance in eating as upon the choice or rejection of certain foods. If feasible, spa treatment may be of service by affording the patient an opportunity to change his diet and mode of life and by teaching him how he must live thereafter. Measures which promote the action of the skin and kidneys should not be neglected. If there is a suspicion that syphilis has played any part in the production of the disease, such drugs as arsphenamin, mercury and iodids, should be given a thorough trial, although it must be recognized that even if the influence of syphilis is unquestioned, no drug can materially affect the cirrhotic process itself. The portal system is

best depleted by saline aperients and the occasional use of a mild mercurial. Mineral waters, such as those of Vittel, Carlsbad, and Hunyadi János, taken hot an hour before meals, sometimes have a good effect.

Ascites, if not speedily relieved by purgatives (salines, compound jalap powder, or blue mass), diuretics (theobromin, theocin, caffein, or digitalis), the Baillie or Niemeyer pill (digitalis, squill and blue mass), and a dry diet, should be tapped. The operation (*paracentesis abdominis*), if done with reasonable care and under aseptic precautions, is virtually devoid of danger. Occasionally, after a number of tappings the fluid does not return for a long period—perhaps several months or even years—generally, however, the abdomen quickly refills and withdrawal of the fluid at short intervals is necessary. The operation is performed as follows: The bladder having been emptied and the skin of the abdomen carefully cleansed, the patient is placed in a semirecumbent position near the edge of the bed. The puncture is usually made in the median line midway between the symphysis pubis and the navel, but if owing to adhesions or other causes the fluid cannot be withdrawn in this situation, it may be made on the left side midway on a line between the symphysis and the anterior-superior spine of the ileum. The area selected for the puncture may be anesthetized, if necessary, by means of a block of ice sprinkled with salt or by a spray of ethyl chloride. The trocar (about $\frac{1}{8}$ inch in diameter) is introduced into the abdominal cavity with a quick thrust and the escaping fluid is then conducted through a rubber tube, attached to the cannula, into a pail placed by the side of the patient's bed. If the flow becomes interrupted, it may often be reëstablished by changing the direction of the cannula or passing into it an aseptic probe. While the fluid is escaping a many-tailed binder should be adjusted to the abdomen and gradually tightened. The binder gives support to the relaxed abdominal wall, and tends to prevent syncope, tympanites and hematemesis. It should be kept on for two or three days. After the fluid has ceased to flow, the cannula is removed, and the wound sealed with a sterile pad and a few strips of adhesive plaster.

**Surgical Treatment.**—The operation having for its object an increase in the anastomotic channels between the radicles of the portal vein and the general systemic veins was originally suggested by Talma of Utrecht in 1889, although it was independently proposed by Drummond of Newcastle-upon-Tyne and first carried out with success by Morison in 1895.[1] It consists in the production of adhesions by scraping and suturing the peritoneal surfaces in the region of the liver and in uniting the omentum to the abdominal wall (epiplopexy). The good effects of the Talma-Morison operation have been ascribed chiefly to the formation of supplemental channels of anastomosis, but it is possible that some of the benefit may be due to lessening of the venous pressure within the liver and improvement in the nutrition of the hepatic cells. Although the mortality of the operation has been high and many failures have been recorded, undoubtedly more gratifying results would have been achieved if greater care had been exercised in the selection of cases. Of 227 cases tabulated by Sinclair White[2] death occurred in 75 (33 per cent.); failure in 34 (15 per cent.); improvement in 29 (13 per cent.); and symptomatic cure, which at the time of publication had lasted from 6 months to 3 years or longer, in 84 (37.3 per cent.). W. J. Mayo[3] reports 28 operations with 4 operative deaths. Eight of the patients died at various times following the operation and 16 were more or less benefitted. The operation should

[1] Brit. Med. Jour., Sept. 19, 1896.
[2] Brit. Med. Jour., Nov. 10, 1906.
[3] Annals of Surg., 1918, lxviii, 183.

be restricted to patients who are less than 55 years of age, who are still fairly well nourished, and who have ascites as the chief symptom, and it should not be undertaken until several tappings have proved ineffectual. Associated cardiac, renal or pulmonary disease, arteriosclerosis, jaundice, and signs of toxemia are contraindications.

Various operations have been devised for draining automatically the ascitic fluid into the subcutaneous cellular tissue or directly into the circulation (autodrainage). Knotte's method, in which the saphena vein is sutured to the peritoneum, has a number of successes to its credit, but as yet no definite conclusions are possible. In cases of hepatic cirrhosis with early and very pronounced enlargement of the spleen and other features suggestive of Banti's disease, splenectomy should be considered. W. J. Mayo[1] has removed the spleen in 6 cases. One patient died soon after the operation and the others were much benefited. He believes that in suitable cases splenectomy is superior to the Talma-Morison operation.

## Biliary Cirrhosis of the Hanot Type

### (Primary Biliary Cirrhosis; Hypertrophic Biliary Cirrhosis)

**Etiology and Pathogenesis.**—Contrasted with portal cirrhosis and obstructive biliary cirrhosis, the form of cirrhosis described by Hanot is decidedly rare. Doubtless, as Mayo has stated, many cases that have been classed as Hanot's disease have been in reality examples of secondary biliary cirrhosis or of hemolytic icterus. The disease is most common in adults between the ages of 20 and 35, although many cases are observed in children. In adult life males are chiefly affected, but in childhood the two sexes suffer about equally. The occurrence of several cases in the same family has been noted by a number of writers. The cause of the disease is not known. Alcoholic excess, syphilis and gross obstruction of the bile-ducts are apparently without etiologic influence. In a considerable number of cases the condition has directly followed one of the specific fevers. In view of this association and the frequency of fever, leucocytosis and general lymph-node enlargement, an infective origin has been suspected, but whether the infective agent or toxin reaches the liver from the intestine through the bile-ducts, producing an ascending cholangitis, or whether it enters the liver from the blood and in the process of excretion sets up a descending cholangitis is not apparent. The comparative infrequency of inflammatory changes in the duodenum and larger bile-ducts, however, is suggestive of a primary hemic infection. Whatever the nature of the irritant or the path it travels in reaching the liver, the consensus of opinion is in favor of the view that a radicular cholangitis is the primary lesion and the fibrotic changes are secondary.

**Morbid Anatomy.**—The liver is much enlarged, usually weighing from 2000 to 3000 grams, and is of a deep yellow or greenish-yellow color. The surface is smooth or finely granular, and the substance dense and firm. Microscopic examination reveals an excess of connective tissue in the form of delicate fibrillæ, that not only pass between individual lobules (monolobular cirrhosis) but in many places enter the lobules and surround small groups of cells (intralobular cirrhosis) or single cells (monocellular cirrhosis). In advanced cases a multilobular (portal) type of cirrhosis sometimes supervenes, bands of connective tissue frequently enclosing and isolating a number of contiguous lobules. A conspicuous feature is the presence of many branching columns of small cuboidal cells in the interlobular connective tissue. These structures (pseudobiliary canaliculi) apparently represent an attempt at

[1] *Ibid.*

the formation of new bile-ducts. Still more characteristic, however, are the changes in the pre-existing bile-capillaries and small bile-ducts. These are of inflammatory nature and comprise proliferation and desquamation of the epithelium and occlusion of the lumen by plugs of inspissated bile. The liver cells often present an almost normal appearance until a late period, but extensive necrosis may supervene at any time and terminate the condition. The interlobular and intralobular branches of the portal vein are unobstructed. In cirrhosis of the portal type, as constrasted with that of the Hanot type, the new connective tissue is coarse and dense, and is chiefly distributed around groups of lobules (multilobular); there is no inflammation of the bile-ducts, and the hepatic cells almost invariably show more or less degeneration and atrophy. It must be admitted, however, that much overlapping occurs and that in some cases the histologic picture bears as much resemblance to one form as to the other.

The spleen in primary biliary cirrhosis is enlarged, commonly weighing between 400 and 600 grams. Occasionally it weighs more than the liver. The lymph-nodes in the portal fissure are also enlarged and rarely there is a more or less general glandular enlargment.

**Symptoms.**—Jaundice is usually the first obtrusive symptom, although it is often preceded for a long time by indefinite gastro-intestinal disturbances. Recurrent attacks of pain and tenderness over the liver, with fever, leucocytosis, and an increase in the jaundice and digestive disturbance are of common occurrence. At first these attacks recur at intervals of months, or perhaps years, but as the disease progresses they become more frequent and last longer, and finally the patient may seldom be free from abdominal pain and fever. The jaundice, though varying in degree from time to time, is rarely so intense as that occurring in chronic obstruction of the larger bile ducts and as proof that some bile still passes into the intestine, the stools retain their dark color. The liver is uniformly enlarged throughout the whole course of the disease, and in the later stages it may extend downward as far as the crest of the ileum. Each paroxysm of pain and fever is followed, as a rule, by some increase in its size. The surface of the organ is smooth and firm. The spleen is also enlarged and in some cases even to a greater degree than the liver. The abdominal veins are rarely distended and ascites is uncommon, except as a terminal feature, and even then it is usually slight. Clubbing of the fingers is occasionally observed in long-standing cases. The general health may be fairly well-maintained for a long period, but eventually weakness and emaciation appear, and if death does not result from some intercurrent disease, the patient passes into a drowsy state that finally develops into coma. Toward the end hemorrhages from the mucous membranes and into the skin may occur. Occasionally the disease is brought to an end in one of the periodic exacerbations, the symptoms suddenly expanding into those of acute yellow atrophy of the liver.

**Diagnosis.**—The history, the periodic attacks of fever and leucocytosis, the marked enlargement of the spleen, and the absence of hematemesis, ascites and other signs of portal obstruction will usually serve to distinguish primary biliary cirrhosis from *portal cirrhosis*, with enlargement of the liver and intercurrent jaundice. In *obstructive biliary cirrhosis* the jaundice is usually deep from the beginning, the stools are pale, the liver is, as a rule, only moderately enlarged, and the spleen is often little, if at all enlarged. *Banti's disease* may offer much difficulty. The occurrence of pronounced splenomegaly, of decided anemia of the secondary type with leucopenia, and of gastrointestinal hemorrhages before the appearance of jaundice is in favor of Banti's disease; while early and pronounced hepatic symptoms, with

recurrent attacks of pain, fever, and leucocytosis are in favor of Hanot's cirrhosis. *Hemolytic jaundice* may usually be distinguished by the acholic urine and the increased fragility of the erythrocytes. *Syphilis of the liver* may readily be mistaken for Hanot's cirrhosis and in many cases a definite diagnosis must rest on the presence or absence of other evidences of syphilis and the results of antisyphilitic treatment. *Gaucher's disease* is attended by enlargement of the liver and spleen and a peculiar brownish discoloration of the skin, but it may be differentiated by the absence of actual jaundice, fever, and leucocytosis, by the presence of a brownish-yellow wedge-shaped thickening of the conjunctiva, and by its strong familial tendency.

**Prognosis.**—The disease is incurable, but it may last from 5 to 10 years or longer, and the patient's health may remain fairly good until a late period.

**Treatment.**—The treatment is largely symptomatic. Hexamethylenamin has been recommended, but it is of doubtful value. Calomel, in doses of $\frac{1}{8}$ to $\frac{1}{4}$ grain (0.008–0.016 gm.), every three or four hours, periodically, for three or four days, has also been extolled (Sacharjin, Goluboff). Drainage of the gall-bladder and biliary ducts is said to have resulted in improvement, and in a few cases of supposed Hanot's cirrhosis splenectomy has been followed by a cure.

## Obstructive Biliary Cirrhosis of the Liver

This term is applied to a more or less diffuse overgrowth of connective tissue in the liver occurring as a sequel to obstruction of the larger bile-ducts and resulting from long-continued stasis of bile and infection of the biliary passages. The disease is usually associated with gall-stones, but it may be produced by tumors that obstruct the bile-ducts and even by chronic non-calculous cholecystitis. Very pronounced cirrhosis of this type occurs also in congenital atresia of the bile-ducts.

**Morbid Anatomy.**—The liver is uniformly enlarged, although usually much less so than in Hanot's cirrhosis. The surface of the organ is smooth or finely granular and its substance is of a yellowish or greenish color. Microscopically, the fibrosis is especially marked about the interlobular biliary capillaries and in the peripheral zones of the acini, where a greater or less number of the original hepatic cells have disappeared. In advanced cases compensatory proliferation of the hepatic cells and new formation of biliary capillaries are observed, as in other forms of cirrhosis. The original bile ducts are dilated, thickened and distorted. Except in long-standing cases the spleen is little, if at all, enlarged. Not infrequently chronic pancreatitis is present as a result of the underlying biliary infection.

**Symptoms and Diagnosis.**—Clinically, obstructive biliary cirrhosis closely resembles cirrhosis of the Hanot type. In the former, however, the primary cause of the disease is almost always in evidence, the icterus is, as a rule, more intense, the stools often being completely devoid of bile, the liver itself is usually only moderately enlarged, and splenomegalia is frequently absent. Obstructive biliary cirrhosis may simulate hemolytic jaundice, but in the latter the stools are cholic and the urine is acholic, the spleen is usually much larger than in biliary cirrhosis, and the resistance of the erythrocytes to hypotonic salt solution is almost always decreased. The absence of any definite cause, the early and pronounced splenomegaly, the appearance of jaundice, and the occurrence of pronounced anemia of the secondary type with leucopenia will usually serve to differentiate Banti's disease from obstructive biliary cirrhosis.

DIFFERENTIAL DIAGNOSIS OF DISEASES PRODUCING ENLARGEMENT OF THE LIVER AND SPLEEN

| | Hanot's cirrhosis of the liver | Obstructive biliary cirrhosis of the liver | Banti's disease | Chronic hemolytic icterus | Gaucher's disease |
|---|---|---|---|---|---|
| 1. Usual time of onset. | Adult life. | Adult life. | Adult life. | Infancy or childhood, but may occur in adult life. | Childhood. |
| 2. History | Usually negative. | *Gall-stones; cholangitis.* | Negative or evidence of syphilis. | *Often congenital and familial.* | Sometimes familial. |
| 3. Liver and spleen | *Pronounced enlargement of liver*, followed by slight or moderate splenomegaly. | *Moderate enlargement of liver*, sometimes, but not usually, followed by slight or moderate splenomegaly. | *Pronounced splenomegaly*, followed by considerable enlargement of the liver. | *Marked splenomegaly* often, but not always, followed by moderate enlargement of the liver. | *Enormous enlargement of the spleen*, often followed by moderate or pronounced enlargement of the liver. |
| 4. Jaundice | Present. | Present. | *Usually absent.* | Present and fluctuating. | *Absent, but skin has a brownish hue and yellowish wedge-shaped thickening appears in the conjunctiva.* |
| 5. Stools | Cholic. | *Usually acholic.* | Cholic. | Cholic. | Cholic. |
| 6. Urine | Cholic. | Cholic. | Acholic. | *Acholic.* | Cholic. |
| 7. Ascites | Rare. | Rare. | *Common.* | Absent. | Absent. |
| 8. Blood changes | Anemia usually absent. | Anemia slight or absent. | *Moderate secondary anemia with leucopenia.* | *Pronounced secondary anemia common, with reticulated red cells in excess and resistance of red cells decreased.* | Moderate secondary anemia with leucopenia. |
| 9. Hemorrhages | Absent. | Absent. | *Common, especially from the gastrointestinal tract.* | Rare. | *Common in the later stages, especially from the mucous membranes.* |

**Treatment.**—The treatment is mainly that of the causative condition. Removal of gall-stones and drainage of the bile-ducts, however, are not always curative. W. J. Mayo[1] has observed marked improvement from splenectomy in a number of long-standing cases with enlargement of the spleen.

## MALIGNANT DISEASE OF THE LIVER

**Incidence.**—Primary carcinoma of the liver is rare, occurring in less than 1 per cent. of all autopsies and constituting about 3 or 4 per cent. of all malignant growths in the liver. Secondary carcinoma is very common, about 40 per cent. of all persons dying of malignant disease having secondary growths in the liver. The primary seat is usually in one of the digestive organs, most commonly the stomach, but it may be in the breast or genito-urinary tract.

Primary sarcoma of the liver is extremely rare, probably less than 60 or 70 undoubted examples being on record. Secondary sarcoma constitutes about 10 per cent. of all malignant tumors in the liver. The most frequent primary seats are the bones, suprarenal bodies, mediastinum, eye and skin. Melanosarcomas are due almost invariably to metastasis of a primary growth in the eye or skin.

Primary malignant disease of the liver is much more common in men than in women, but metastatic growths are slightly more common in women than men. Both forms occur usually after 40 years of age, although a number of cases both of primary carcinoma and of primary sarcoma in children have been reported.

**Morbid Anatomy.**—As pointed out by Eggel[2] in a critical study of 163 cases, primary carcinoma appears in three forms: (1) Nodular, the usual form, consisting of scattered nodules of variable number and size; (2) massive, in which there is a single large mass occupying the greater part of a lobe and often surrounded by several small metastatic nodules and (3) diffuse, in which the whole organ is infiltrated with very minute cancer nodules each enclosed in a connective tissue band (carcinomatous cirrhosis), differentiation from pure cirrhosis often being impossible without the aid of the microscope. The right lobe is affected more frequently than the left. Histologically, two groups are recognized: (*a*) simple carcinoma, with solid cell masses and (*b*) adenomatous carcinoma, with the epithelium arranged in glandular form. In either case the tumor may be derived from the liver cells or the epithelium of the bile-ducts. Cirrhosis is a common feature in all forms of primary carcinoma, and according to many observers (Eggel, Orth, Rolleston) it precedes the tumor formation, the epithelial proliferation of the cirrhosis sometimes overshooting the mark and becoming atypical. If the fibrotic change is extensive the liver may be but little, if at all, enlarged. Tumor thrombosis of the portal and hepatic veins is common in primary carcinoma and so also are metastases, not only within the liver itself, but also in other organs, especially the lungs.

Secondary carcinoma arises by direct extension from a contiguous structure, such as the gall-bladder or bile-duct, or by metastasis, in which case the transmission of the cancer-cells is effected through the blood vessels, usually the portal vein. Metastatic growths are in the form of multiple grayish

[1] Jour. Amer. Med. Assoc., 1918, lxx, 1361.
[2] Beitr. z. path. Anat. u. z. allg. Path., 1901, xxx, 506.

nodules, some of which project from the surface of the organ as slightly elevated bosses. As a result of necrotic changes in the interior, the center of the boss is often depressed (umbilicated). The liver as a whole may be enormously enlarged.

Primary sarcoma may occur either as a massive or as a nodular growth; secondary sarcoma may be nodular or diffuse.

**Symptoms.**—The symptoms of malignant disease of the liver do not differ materially whether the growth be primary or secondary, carcinomatous or sarcomatous. In many cases, especially of secondary carcinoma, there is no clinical evidence that the liver is affected. On the other hand, in a large proportion of cases of secondary malignant disease the primary growth remains latent and the symptoms are almost exclusively hepatic. As a rule, there is more or less disturbance of digestion and for a time this may be the chief manifestation. Pain, although it is by no means a constant symptom, is usually present at some period of the disease. It may be due to stretching of the capsule or to localized peritonitis. In some instances it is more severe in the back than in the right hypochondrium, and not infrequently it is referred to the right shoulder or even to the right arm. Jaundice occurs in more than one-half of the cases. It is sometimes due to compression of the intra-hepatic ducts by cancerous nodules, and if so, it is commonly persistent, but not so intense. Occasionally it depends upon associated cholangitis and in such a case it may be only temporary. As a rule, however, it is due to compression of the common bile-duct by enlarged lymph-nodes in the portal fissure or by a primary growth in an adjacent organ, and hence it is usually permanent and in the later stages very deep. Ascites is also common, but relatively less frequent than jaundice. It may be due to compression of the portal vein or occlusion of the vessel by a cancerous thrombus, or to chronic peritonitis.

Progressive enlargement of the liver is the most important physical sign. The enlargement involves chiefly the right lobe and in many cases reaches enormous proportions. On palpation the organ is usually firm, tender and characteristically nodular. Depressions in the nodules may occasionally be made out. The gall-bladder is frequently distended and in some cases, particularly of cancerous cirrhosis, the spleen is also enlarged. Small secondary nodules are rarely palpable in the subcutaneous tissues of the abdominal wall, especially about the unbilicus. A right-sided pleuritic effusion, usually hemorrhagic, sometimes develops in consequence of the extension of the growth through the diaphragm. The blood shows the changes of secondary anemia. The urine contains an excess of urates and in cases of melanotic sarcoma it may also contain melanin. Nor rarely slight remittent or intermittent fever is present as a result of auto-intoxication or complicating infection. Weakness, emaciation and cachexia eventually develop; secondary growths sometimes appear in other organs, especially the lungs; and toward the close there may be somnolence and other toxic phenomena, attributable either to hepatic insufficiency or to jaundice.

**Diagnosis.**—Rapid and progressive enlargement of the liver, with palpable nodules, local pain and tenderness, and increasing loss of flesh and strength are the chief points on which to base a diagnosis of malignant disease of the liver. The presence of jaundice, ascites and signs of a primary growth elsewhere are additional and conclusive evidence. The differential diagnosis between primary and secondary carcinoma may be extremely difficult, owing to the frequency with which small primary tumors in the stomach, pancreas or esophagus remain latent. Primary carcinoma may be suspected, however, if the tumor is single, the course is very rapid, and there is no indication of

cancer in any other organ. The exclusion of *primary carcinoma of the gall-bladder or of the larger bile-ducts* is often impossible. The former would be suggested by the history of gall-stones and the original appearance of the tumor in the region of the gall-bladder, and the latter, by steadily increasing jaundice and cachexia without enlargement of the liver or symptoms of cancer elsewhere. *Syphilis of the liver* is readily confused with carcinoma. A relatively marked enlargement of the left lobe as compared with the right, persistent fever, palpable enlargement of the spleen and a prolonged course with periodic remissions are in favor of syphilis, but the decisive points are the proof of infection and the results of specific treatment. *Hepatic abscess* is likely to come into question only in those cases in which the cancerous nodules soften and fever is present. The antecedent history is often of great assistance in the diagnosis. Wide fluctuations of temperature, pronounced leucocytosis, and absence of cachexia are in favor of abscess; the association of jaundice and ascites is strongly suggestive of cancer. In *obstruction of the common bile-duct by a calculus* as contrasted with malignant disease the jaundice is usually subject to periodic variations in intensity, malaria-like paroxysms are common, the liver is only slightly enlarged, and for a long time there may be no marked deterioration of the general health. Persistent, gradually deepening jaundice with distention of the gall-bladder, nodular enlargement of the liver, and ascites point to carcinoma.

**Prognosis.**—Malignant disease of the liver is inevitably fatal, usually within a year of its recognition. Occasionally death occurs in the course of a few weeks. The only exceptions to this statement are the extremely rare instances in which recovery has followed the removal of a single primary growth or one that has invaded the liver from the gall-bladder.

**Treatment.**—Except in the rare cases in which an exploratory incision shows operation to be practicable, treatment has to be confined to the relief of symptoms, especially of pain. According to Yeomans,[1] 16 operations for primary carcinoma were recorded up to 1914, and 6 of the patients were alive and well from 3 to 7 years after operation.

## BENIGN TUMORS AND CYSTS OF THE LIVER

**Benign Tumors.**—Solitary adenoma, lipoma, and fibroma are occasionally observed, but are without clinical importance. Angioma is the most common primary tumor of the liver. As a rule, it is small and produces no symptoms. Occasionally, however, it attains an enormous size and causes enlargement of the abdomen, ascites and edema of the legs. Major and Black[2] describe an hepatic angioma weighing 40 pounds (18,160 grams), Pfannenstiel,[3] one weighing more than 11 pounds (5290 grams), McWeeney[4] one weighing more than 11 pounds (5,100 grams), and Payne[5] one weighing 6 pounds (2700 grams).

**Cysts.**—Simple cysts are usually single and comparatively small. They are probably caused by local obstruction of the bile-ducts. Polycystic disease of the liver is rare and usually associated with a similar condition in the kidneys. Other malformations may also be present. Whether the cystic

[1] Jour. Amer. Med. Assoc., April 17, 1915.
[2] Amer. Jour. Med. Sci., 1918, No. 4, 469.
[3] Allg. med. Centr. Ztg., 1898, lxvi.
[4] Jour. Path. and Bacteriol., 1911–1912, xvi, 401.
[5] Trans. Path. Soc., London, 1869, xx, 203.

change represents a developmental defect, is of neoplastic origin, or is a result of fetal cholangitis is not known. There are no characteristic symptoms. The most important cyst of the liver is the echinococcus cyst, which is produced by the scolex of *Tænia echinococcus* (see p. 308).

## ACUTE YELLOW ATROPHY OF THE LIVER

**Definition.**—Acute yellow atrophy of the liver is an acute diffuse necrosis of the liver cells of varying etiology, but probably always of toxic or infectious origin, characterized clinically by reduction in the size of the liver, jaundice, and profound toxemia, and usually proceeding to a fatal issue.

**Etiology.**—Typical acute yellow atrophy is rare, even in the largest hospital practice often a decade passing without one case being observed. No period of life is exempt, but the disease is commonest between the ages of 20 and 30, and females are more often attacked than males, the proportion being about 2 to 1. This greater incidence in women is due, at least in part, to the important influence of pregnancy, a large proportion of the cases occurring during gestation (usually the second half) or soon after childbirth. Even in pregnancy, however, the fully developed condition is rare. A close relationship appears to exist between pernicious vomiting of pregnancy and acute yellow atrophy of the liver, and various gradations between these two complications have been observed. Certain infections, especially syphilis, are of undoubted etiologic significance. The mild jaundice sometimes observed in secondary syphilis is occasionally followed by the disease. In 1911 Umber[1] collected 50 cases of post-syphilitic acute yellow atrophy. Of 40 cases of jaundice in early syphilis, analyzed by Michael,[2] 10 per cent. went on to acute yellow atrophy. Testimony from various sources shows conclusively that the disease may proceed from infectious jaundice, whether sporadic or epidemic. The reported outbreaks of acute yellow atrophy limited to small communities or even to households apparently have had this origin. Certain non-bacterial poisons, such as alcohol and chloroform, may also stand in causal relationship to the disease. In 6 of Thierfelder's[3] 143 cases the attacks followed an alcoholic debauch. The resemblance of acute yellow atrophy to delayed chloroform poisoning, both as regards the clinical picture and the pathologic changes, is striking, and Campbell-Horsfall[4] cites reports of 11 cases following operation, in nearly all of which chloroform had been used as an anesthetic. Poisoning with trinitrotuolol, picric acid, and other benzene derivatives has also been reported as a causal factor (Stewart, Crawford[5]). Phosphorus poisoning closely resembles acute yellow atrophy, but the two conditions are probably not identical, as the former, unlike acute yellow atrophy, always leads to a great excess of fat in the liver and nearly always to marked enlargement of the organ.

The disease occasionally follows the administration of arsphenamin for luetic infection, but it is not always clear whether the hepatic changes are induced by the arsenic or are the result of the syphilis. In a few instances, as in one reported by Curschmann,[6] the disease has followed close upon

[1] Münch. med. Woch., 1911, 58, 2499.
[2] Arch. f. Dermat. u. Syph., 1914, 120, 694.
[3] v. Ziemssen's Cyclopedia, 1880, ix.
[4] Lancet, Sept. 7, 1907.
[5] Brit. Med. Jour., April, 20, 1918.
[6] Münch. med. Woch., 1915, lxii, No. 52.

traumatic injury of the liver. In view of the frequency with which the condition has supervened upon some other disease of the liver, such as cirrhosis or cholangitis, it is likely that impaired resistance on the part of the hepatic cells is an important disposing factor.

**Morbid Anatomy and Pathogenesis.**—The liver is diminished in size, often weighing only one-half or one-third of its normal weight (800–500 grams). The capsule is wrinkled; the organ itself is flabby, but rather tough. On section, the cut surface is yellow, with here and there reddish areas, which are somewhat depressed. The lobular markings are indistinct or absent. Microscopic examination of the yellow areas, in which the changes are more recent, shows various grades of degeneration in the parenchymatous tissue. The cells, especially those near the centers of the lobules, are swollen, granular, and infiltrated with bile-pigment and are without visible nuclei. The yellowish coloration is due to the pigment rather than to any excess of fat. In the red areas the liver cells have largely or completely disappeared, leaving behind fields of granular detritus, traversed by the original stroma and a network of capillaries. Hemorrhagic foci are often present. The small bile-ducts are filled with detached epithelium. In the less acute cases evidences of inflammatory reaction and of regeneration may be seen in the form of small-cell infiltration, columns of cells resembling small bile-ducts (pseudobiliary canaliculi) and islets of cells with deeply staining nuclei, manifestly derived from surviving hepatic cells.

Chemical examination of the fresh hepatic tissue shows the presence of leucin and tyrosin and other products of proteolysis in considerable quantities, but little or no increase in the fat content.

The gall-bladder is not distended and the larger bile-ducts are patent. The lymph-nodes at the hilum are sometimes swollen, the kidneys and heart show evidences of cloudy swelling, and the spleen is often softened and enlarged. Small hemorrhages are frequently found in the skin, beneath the pleura and pericardium, and in the mucous membranes. Ascites was present in 20 per cent. of 33 cases observed by E. Fraenkel.[1]

Although the nature of acute yellow atrophy is still obscure, it can scarcely be doubted that the disease is due to some poison, which is sufficiently virulent in itself to cause rapid destruction of the parenchymatous cells of the liver or which becomes capable of producing this effect when the resistance of the hepatic tissue has already been reduced by other means. The change in the hepatic cells, which from the outset is a necrotic one, begins in the centers of the lobules and spreads outward, ultimately involving entire lobules in large areas of the organ. In the rapidity and completeness with which the affected cells are dissolved and removed, without the aid of leucocytic infiltration, the process closely resembles the self-digestion occurring in dead but aseptic tissues, such as anemic infarcts, and for this reason the suggestion has been made that the poison kills the cells without injuring their proteolytic enzymes, and consequently autolysis ensues (Wells[2]). The jaundice of acute yellow atrophy is probably due to disorganization of the biliary capillaries and the escape of the bile into the blood (Mac Callum[3]), although as there is increased hemolysis the production of large quantities of thick, viscid bile may result in blocking of the minute ducts and reabsorption of the bile. The leucin and tryosin found in the liver and also in the urine are probably derived in part from autolysis of the hepatic cells and in part from amino-acids which have been formed in the intestine and elsewhere and which have not been converted into urea in the liver.

[1] Deutsche med. Woch., 1920, 46, 225.
[2] Wells: Chemical Pathology, Phila., 1920, p. 547.
[3] Mac Callum: A Text-book of Pathology, Phila., 1920, p. 316.

**Symptoms.**—In the majority of cases there is an initial stage of a few days duration in which the symptoms are indistinguishable from those of ordinary gastroduodenitis with catarrhal jaundice. Very soon, however, there is a marked change for the worse in the patient's condition. The jaundice deepens; the vomiting becomes more severe and the vomited matter may contain blood; extreme restlessness and irritability supervene, and are rapidly followed by delirium, which is usually violent and maniacal, but which may be low and muttering throughout. Often muscular twitchings occur and occasionally there are actual convulsions. The tongue is dry and brown, the pulse is frequent and weak, the respirations are accelerated and irregular, the pupils are, as a rule, dilated, hemorrhages often occur in the skin and from various mucous membranes, and if the patient be a pregnant woman, abortion results. In a short time, usually in from 2 to 3 days, stupor ensues and rapidly develops into coma. There is usually an absence of fever until just before death when the temperature may rise to 104° or 105° F.

With the onset of the severe symptoms the area of liver dulness diminishes, the diminution being partly due to wasting of the organ and partly to its flabbiness, which allows it to fall away from the ribs. The spleen is often enlarged. Moderate leucocytosis may be present. The urine is scanty and contains bile pigments, and, as a rule, albumin and tube-casts, but the most significant urinary changes are the presence of amino-acids in considerable quantities, especially leucin and tyrosin, the presence of various fatty acids, and the increased excretion of ammonia at the expense of urea. The excess of ammonia may depend upon the failure of the liver to convert ammonium compounds into urea or it may be the consequence merely of the acidosis, which it tends to neutralize.

Certain departures from the usual type are sometimes observed. Thus, the onset is occasionally sudden with an outbreak of violent delirium, suggesting meningitis or mania; in rare instances jaundice is absent throughout, although the other characteristic symptoms are present; and in exceptional cases, probably owing to some preëxisting hepatic lesion, the liver may be found enlarged, even in the later stages.

**Course.**—Pronounced attacks of acute yellow atrophy almost always end fatally, death occurring, as a rule, within a fortnight from the onset or a few days from the occurrence of the grave cerebral symptoms. Sometimes, however, the course extends over several weeks, and occasionally in these less acute cases partial or even complete recovery ultimately occurs.

**Diagnosis.**—Once the disease is fully developed the diagnosis is easy, the association of deep jaundice with severe nervous symptoms, diminished liver dulness, and leucin and tyrosin in the urine being characteristic. In *phosphorous poisoning* there is usually the history of the ingestion of a poison, the vomiting at the onset is more severe, the vomitus may contain phosphorus, and the liver almost always remains enlarged. In suppurative cholangitis the jaundice is accompanied by fever and chills and the liver dulness is increased.

**Treatment.**—There is no treatment of much avail. A diet of milk, well diluted with lime-water or carbonated water, free purgation, intravenous or subcutaneous injections of normal salt solution, the administration of sodium bicarbonate by the mouth, or, if necessary, intravenously (2 per cent.), and the use of enemas containing dextrose (5 per cent.) have been recommended to combat the acid intoxication. Cold applications should be made to the head to relieve nervous symptoms and bismuth subcarbonate, diluted hydrocyanic acid, or effervescing drinks should be given to allay vomiting.

## FATTY LIVER

The term "fatty liver" is used to designate the two conditions usually described as fatty infiltration and fatty degeneration respectively. In fatty infiltration there is an excessive accumulation of fat in cells otherwise normal or only slightly changed. In fatty degeneration there is a primary breaking down of the cells accompanied by a deposit of fat, although the latter, contrary to what was formerly believed, is probably not a product of the disintegrating cells themselves, but an import from the usual fat depots in other parts of the body. Neither process, however, is common in pure form, higher grades of fatty infiltration always being associated with some retrograde change in the cell protoplasm and fatty degeneration, even when not advanced, being almost invariably accompanied by increased deposition of fat. For this reason the two changes may be considered together.

**Etiology.**—The chief causes of fatty liver are: (1) The various factors that tend to produce obesity such as the ingestion of inordinate amounts of food rich in fats and carbohydrates, muscular inactivity, anomalies of internal secretion, etc.; (2) diseases that reduce the oxidative processes in the body, such as chronic anemia, pulmonary tuberculosis, etc.; (3) severe infections, such as septicopyemia, the acute exanthemata, typhoid fever, etc.; (4) various non-bacterial intoxications, as by alcohol, phosphorus, arsenic, chloroform, etc.

**Morbid Anatomy.**—As a rule, the organ is large, uniformly smooth, of a yellowish color and of doughly consistence. A dry knife passed through it becomes coated with fat. Histologically, the cells contain large or small drops of fat. When the change is a simple infiltration the fat is commonly in the form of a large globule which presses the nucleus to one side, giving rise to the so-called seal-ring appearance; where as in well-marked degeneration the fat is usually, but not invariably, in the form of minute particles uniformly scattered through the cytoplasm and the nucleus shows evidences of disintegration. In the majority of cases the changes partake of the nature of both processes.

**Symptoms.**—Fatty changes in the liver do not often seriously disturb the functions of the organ, and when subjective symptoms are present, they are usually those of associated lesions or of the primary condition that affected the nutrition of the liver. Occasionally the patient complains of a sense of fullness or weight in the right side and of some derangement of digestion. In the presence of one of the exciting causes, a fatty liver may be suspected if the organ is large, smooth, and of normal shape, and there are no indications of obstruction to the bile-ducts or portal circulation. In thin subjects, the soft consistence of the enlarged liver and its rounded margin afford additional evidence of fatty change. In the differential diagnosis one must exclude cirrhosis, amyloid disease, leukemic infiltration, passive congestion, morbid growths, and displaced liver.

**Treatment.**—The treatment is that of the primary cause.

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## AMYLOID LIVER

The retrogressive process, described as lardaceous by Rokitansky (1842), waxy by Christensen (1844), and amyloid by Virchow (1854), is characterized by the deposition in the tissues of a glass-like material, which according to Krawkow,[1] is a combination of a protein with chondroitin—sulphuric

[1] Arch. f. exp. Path. u. Pharm., 40, 1897.

acid, the interaction between the two probably taking place *in situ*. The deposit is usually widespread, affecting a number of organs, but is most pronounced, as a rule, in the spleen, kidneys and liver.

**Etiology.**—The causes of amyloid disease of the liver are those of amyloid change in general, namely, certain chronic disorders associated with severe anemia and progressive wasting, the most important being chronic tuberculosis, especially of the bones and joints, with cold abscess formation, and chronic ulcerative syphilis. More rarely it develops in the course of non-suppurative affections, such as leukemia, carcinoma, malarial cachexia, and chronic nephritis. Experimentally, it may be produced in animals by repeated injections of various bacteria or their toxins, especially an attenuated staphylococcus culture, or the maintenance of aseptic suppuration by means of turpentine. Owing to improved methods of treatment which eliminate protracted suppuration, advanced amyloid disease is relatively infrequent at the present time.

**Morbid Anatomy.**—The liver is uniformly enlarged, dense, and heavy. The surface is smooth and the margins are blunt. Upon section the tissue is pale, and, if the process is well advanced, semitranslucent or wax-like. If a solution of iodin (Lugol's solution) be poured upon it, after washing to remove the blood, the amyloid portions take on a mahogany-brown color and the non-amyloid portions become yellow. Microscopic examination shows that the intermediate zone of the lobule is first affected and that the amyloid material is deposited in the capillary walls external to the endothelium and also in the media of the arterioles. As the process advances the deposit extends both peripherally and centrally, compressing more and more the hepatic cells. The latter are not subject to the amyloid change, but in consequence of compression and narrowing of the vessels, they often show evidences of fatty degeneration and atrophy and may ultimately disappear. If a microscopic section of the tissue be treated with an aqueous solution of methyl-violet, and then washed in acetic-acid water, the amyloid material will be stained rose-pink, while the surrounding tissue will acquire a bluish-violet hue.

**Symptoms.**—Slight degrees of amyloid infiltration cannot be detected clinically, and even when the process is well advanced, its presence may be masked by symptoms of the primary disease. The patient is, as a rule, pale, cachectic, and more or less emaciated. Ascites sometimes occurs either as an independent effusion or as a part of a generalized edema, but it is due rather to the cachexia or some concomitant disorder (peritonitis, hepatic cirrhosis, nephritis) than to the amyloid process itself. As the bile-ducts remain patent throughout there is no jaundice. Digestive disturbances, however, are common, and if the intestines are also involved in the amyloid change there may be intractable diarrhea. The urine is often abundant, of low specific gravity, and albuminous, owing to the participation of the kidneys in the process. Physical examination reveals a large, firm, painless liver, with the contour unchanged, the surface smooth, and the margin usually rounded. Exceptionally, the organ may be doubled in size. In the majority of cases the spleen also is enlarged and presents a firm blunt edge, the changes affecting it being the same as those operating in the liver.

**Diagnosis.**—The diagnosis rests upon the presence of a disease capable of setting up the amyloid change and the occurrence of an enlarged liver having the characteristics already described, in association with increasing cachexia and indications of amyloid infiltration in other organs.

**Prognosis and Treatment.**—Amyloid infiltration is usually a terminal condition and patients rarely recover from the disease in which it occurs;

nevertheless, it is conceivable that in mild cases partial or even complete cure may ensue if the underlying cause is wholly removed. The treatment is altogether that of the primary disease.

# DISEASES OF THE PANCREAS

## PANCREATIC HEMORRHAGE

Hemorrhage into the pancreas in the form of petechiæ may occur in passive congestion of the organ, in various hemorrhagic and infectious diseases, and in certain intoxications. Large hemorrhages are a common sequence of acute pancreatitis and may also occur as a result of physical injury, or spontaneously (*pancreatic apoplexy*) in consequence of sclerosis of the pancreatic arteries. Occasionally, profuse bleeding occurs in the absence of any discoverable cause. Even in such cases it is possible that infection is the inciting factor.

Profuse hemorrhage into the pancreas produces all the phenomena of acute fulminating pancreatitis. It is marked by the sudden occurrence of agonizing pain in the upper part of the abdomen, persistent vomiting, and collapse. The epigastric region is usually distended and resistant to palpation, the face and extremities are often cyanotic, and not rarely the vomitus or the stools contain blood. Exceptionally sugar occurs in the urine. The disease is almost always fatal, death occurring in from a few hours to several days, although recovery with localization of the blood in the form of a cyst is not impossible.

## ACUTE PANCREATITIS

**Definition.**—Acute pancreatitis in its fully developed form is a somewhat uncommon disease, characterized anatomically by necrosis of the pancreatic tissues, with hemorrhage and often gangrene or suppuration, manifested clinically by severe pain in the epigastrium, vomiting, and profound collapse, and proceeding in many instances to a fatal issue.

**Etiology.**—Acute pancreatitis occurs usually in adults, and is most common between the ages of 30 and 60, Males are said to be more often attacked than females, but Linder reports 76 per cent. females in a series of 33 cases, and Deaver[1] 73 per cent. females in a series of 11 cases. Fat persons and those addicted to the use of alcohol appear to be especially prone to the disease. Calculous or non-calculous cholecystitis is present in the large majority of cases. Next to cholecystitis, gastro-intestinal diseases, especially gastric or duodenal ulcer and duodenitis, are the most frequent antecedents. Traumatism is the determining factor in a small proportion of cases. Among the less common causes are the specific fevers, particularly typhoid fever, scarlet fever and mumps. Cases following mumps usually are mild and terminate in recovery. Severe attacks are often preceded by slight ones of a similar character and not rarely the disease supervenes upon chronic interstitial pancreatitis.

[1] Surg. Clin. of North America, Feb., 1921.

**Pathogenesis.**—The mode of production of acute pancreatitis has not been definitely determined, at least for all cases. Undoubtedly, the changes largely depend upon activation of the ferments of the pancreas, in particular of trypsin and lipase, within the gland and self-digestion of its tissues. Activation of the ferments within the ducts may be caused by bile, hydrochloric acid, intestinal juice, or bacterial products. There is reason to believe that regurgitation of bile into the pancreatic ducts, made possible by the impaction of a gall-stone in the ampulla of Vater, may produce acute pancreatitis, even in the absence of bacteria, but the evidence is against the assumption that such a reflux of bile is the sole cause of the disease, except in rare instances. Archibald,[1] has recently suggested that retrojection of bile into the duct of Wirsung, as a result of a powerful contraction of Oddi's sphincter at the ampulla in response to irritation arising in the surrounding viscera, is the essential factor in some cases. While it is likely, therefore, that acute pancreatitis may be brought about in more than one way, many facts educed from clinical and experimental studies favor the view that in the majority of cases the disease is a consequence of bacterial infection, the bacteria lessening the resistance of the pancreatic tissues and at the same time activating the pancreatic enzymes, which in turn cause digestion of the enfeebled gland. Some of the products (proteoses) of such self-digestion are very toxic and are probably responsible for the serious constitutional disturbances occurring in the disease (Whipple[2]). Infection may occur by contiguity from adjacent structures, through the pancreatic ducts, or through the blood stream, but it probably occurs most frequently, as Deaver and Arnsperger have suggested, by way of the lymphatics, free communication existing between the lymphatics of the pancreas and those of the gall-bladder, bile-ducts, stomach and duodenum.

**Morbid Anatomy.**—The changes vary with the intensity and duration of the process. In very mild cases the pancreas is found to be enlarged, firm, and congested. Hemorrhage may be absent or limited to punctate extravasations scattered throughout the organ. The glandular cells are swollen and granular, and the interstitial tissue is more or less infiltrated with leucocytes. Small areas of necrosis are sometimes present. In well-developed cases hemorrhage into the pancreatic tissues is an almost constant feature. The organ is enlarged, of dark purple color, and usually, as a result of necrotic changes, softened. The hemorrhagic area may be sharply circumscribed, but not rarely the extravasation involves a large part of the gland, and even the tissues around it. In addition to the hemorrhage there is more or less extensive necrosis of the pancreatic tissues, not only of glandular cells, but also of the interstitial tissue and bloodvessels. In some instances the dead tissue is soon transformed into a reddish-brown or grayish-black foul-smelling mass (*gangrenous pancreatitis*). If the patient has survived for several days evidences of inflammatory reaction are found at the margins of the necrotic patches. A blood-stained effusion is usually present in the peritoneal cavity and, as a rule, the periglandular fat and the adipose tissue of the omentum and mesentery are dotted over with foci of fat necrosis, their opaque tallow-like appearance contrasting sharply with the translucent yellow of the normal fat. Fat necrosis has been shown to be due to the splitting of fats into fatty acids and glycerin by the lipase that has escaped into the tissue from the pancreatic juice, the glycerin being absorbed, and the fatty acids deposited within the fat cells. Later, according to Langerhans, the fatty acids combine with calcium salts to form soaps.

[1] Surg., Gynec. and Obstet., 1919, xxviii, 529.

[2] Jour. Exp. Med., 1913, xvii, 286, 307; 1916, xxiii, 123; 1917, xxv, 231.

In other cases, especially in those that are less acute, necrosis and hemorrhage are followed by suppuration, a circumscribed abscess resulting or the whole organ being infiltrated with pus. The abscesses may penetrate the lesser or greater peritoneal cavity, may rupture into the stomach or bowel, or may invade the retroperitoneal space and ultimately point beneath the diaphragm (subphrenic abscess) or in the pelvis. Abscesses are occasionally found in the pancreas without any evidence of hemorrhage or fat necrosis, as a result of a primary suppurative pancreatitis.

**Symptoms.**—Mild attacks often precede the severe ones, but almost invariably escape recognition, their chief symptoms, pain in the upper abdominal region and vomiting, usually being ascribed to biliary colic or to some gastric disorder. Severe attacks begin suddenly with intense pain in the epigastrium, soon followed by vomiting and symptoms of profound collapse. The pain is usually continuous with periodic exacerbations and frequently radiates to the back and to the right or left hypochondrium. The vomiting is persistent and not rarely accompanied by hiccough. The extremities are cold, the pulse is rapid, weak and thready, and the expression anxious. Lividity of the face is often a conspicuous feature. The bowels are obstinately constipated. Physical examination of the abdomen reveals distention, tenderness and muscular rigidity, all of which are especially marked in the epigastrium. After the lapse of a few days, if the patient survives so long, an indefinite mass may sometimes be felt above the umbilicus. The mind usually remains clear throughout, but muttering delirium may develop, particularly in the less acute cases. Jaundice, due to pressure of the swollen pancreas on the bile-duct, to duodenal catarrh, or to obstruction of the common bile-duct by a gall-stone, is sometimes present, and hematemesis or melena occasionally results from the escape of blood into the stomach or duodenum. A moderate leucocytosis is usually observed. The urine is often scanty and albuminous, but only rarely contains sugar. In some of the less severe cases the acute symptoms subside in the course of a week or ten days and are followed by evidences of suppuration—irregular fever, sweats, and chills—and the appearance of a definite tumor in the region of the pancreas.

**Course and Prognosis.**—Mild cases frequently end in recovery. Cases characterized by intense pain and pronounced collapse almost always end fatally unless treated surgically. Death may occur within a few hours, but usually it is delayed for 3 or 4 days, and in suppurative cases it may not ensue for several weeks. Even under surgical treatment the mortality is high. Körte records 16 operations with 5 deaths, Balch and Smith[1] 11 operations with 8 deaths, and Deaver[2] 17 operations with 4 deaths. Patients may survive the operation and die afterward from suppuration, secondary hemorrhage, or exhaustion.

**Diagnosis.**—This is difficult and in most cases impossible. Acute pancreatitis should be suspected however, when a patient who has been previously healthy or who has suffered from attacks of indigestion or of biliary colic is suddenly seized with intense pain in the epigastrium, followed by persistent vomiting and profound collapse, and later by tenderness and resistance in the region of the pancreas. The differential diagnosis must be made from acute intestinal obstruction, perforation of the hollow viscera, biliary colic, acute appendicitis, ruptured tubal pregnancy, irritant poisoning, and embolism of the mesenteric arteries.

In *intestinal obstruction* general tympanites is an early phenomenon, but

[1] Pub. of Mass. Gen. Hosp., Oct., 1911.
[2] *Ibid.*

muscular rigidity is late in appearing and so usually are symptoms of collapse; the vomiting often becomes fecal, bowel evacuations are persistently absent, and even the escape of flatus is arrested. In *perforation of the hollow viscera* distention, rigidity and tenderness more rapidly become general, vomiting is at first less pronounced, and the pain is less subject to paroxysmal exacerbations and rarely remains so intense as in pancreatitis. *Biliary colic* sometimes simulates acute pancreatitis, but in the former the general symptoms are, as a rule, less grave, tenderness and muscular rigidity are confined to the region of the gall-bladder, tympanites is delayed and less marked, and the ceaseless unrest of the patient is in striking contrast to the immobility observed in pancreatitis. An initial rigor with a slight rise of temperature is also in favor of biliary colic. *Fulminating appendicitis* sometimes suggests acute pancreatitis, but it may usually be recognized by the localization of the pain, tenderness, and muscular rigidity, and by the absence of early collapse. In *ruptured tubal pregnancy* the history is significant, the pain is less intense and is accompanied by pallor, faintness, air-hunger, sighing, restlessness and other indications of severe hemorrhage; there is often a bloody discharge from the vagina, and the fullness is in the lower part of the abdomen. *Irritant poisoning* may usually be recognized by the history of the case, the more diffuse abdominal pain, and the occurrence of diarrhea instead of constipation. The diagnosis of *embolism of the mesenteric arteries* can rarely be made with certainty, but it may be suspected if there is evidence of vegetative endocarditis or aneurysm, and the pain and vomiting are accompanied by a profuse bloody diarrhea.

**Treatment.**—Operation consisting of exposure of the pancreas and free drainage should be performed as soon as possible after the onset of the disease. Fortunately it is not necessary that the diagnosis should be made with absolute certainty before the abdomen is opened since the conditions most likely to be confused with acute pancreatitis also demand immediate surgical treatment.

## CHRONIC PANCREATITIS

**Varieties.**—Chronic pancreatitis is characterized by a proliferation of the interstitial connective tissue and more or less atrophy of the parenchymatous cells of the pancreas. Following Opie,[1] whose studies have thrown much light upon the nature of pancreatic diseases, most writers recognize two forms of chronic pancreatitis: One in which the newly formed fibrous tissue is chiefly between the lobules (*interlobular*); the other with the new growth of interstitial tissue invading the lobules and penetrating between the acini (*interacinar*). It must be admitted, however, that mixed types are by no means uncommon.

**Etiology.**—The large majority of cases occur in the middle decades of life and males are more frequently affected than females. From two-thirds to three-fourths of the cases of chronic interlobular pancreatitis are secondary to diseases of the biliary passages, chiefly gall-stones. Ulcer of the stomach or duodenum and chronic duodenitis are the next most common antecedents. In both groups of cases infection by way of the lymphatics or the pancreatic ducts is probably the essential cause, although stasis of the pancreatic secretion may be an important contributing cause, the most intense grades of the disease occurring in association with obstruction of the duct of Wirsung by

[1] Diseases of the Pancreas, 1903.

gall-stones in the diverticulum of Vater, morbid growths or pancreatic calculi. Etiologic significance is also attributed to alcoholism, and not rarely cirrhosis of the liver and chronic pancreatitis are associated. In pigmentary cirrhosis of the liver there is almost always fibrosis of the pancreas (21 of 22 cases collected by Anschutz[1]), but the underlying cause of this condition is not known. In some instances chronic pancreatitis is referable to syphilis and occasionally it seems to depend upon arteriosclerosis.

The etiology of chronic interacinar pancreatitis is not, as a rule, evident. In a small group of cases it develops simultaneously with cirrhosis of the liver, probably as a result of the same underlying cause, and in another small group of cases it seems to be the consequence of arteriosclerosis. The studies of Warthin and Wilson[2] indicate that syphilis is sometimes a factor.

**Morbid Anatomy.**—In many cases the pancreas presents no noteworthy macroscopic changes. In well marked chronic interlobular pancreatitis, however, the head of the gland, and sometimes the entire organ, may be enlarged and indurated. In a case reported by Bosanquet the pancreas weighed 454 grams. In other instances the organ is considerably shrunken, and occasionally it is reduced to a narrow band of fibrous tissue traversed by the dilated duct. Microscopically, the interlobular form is characterized by the appearance of coarse strands of connective tissue between the lobules or groups of lobules, and more or less atrophy of the secreting parenchyma. The cells forming the islands of Langerhans, however, are not affected except in very advanced stages of the disease. In chronic interacinar pancreatitis the pancreas is often diminished in size and tougher than normal. Microscopically, the interlobular tissue and secreting parenchyma may not be unaffected, but the characteristic features are an overgrowth of interstitial tissue within the lobules and between the individual acini, and very early degeneration of the islands of Langerhans.

In chronic interlobular pancreatitis disturbances due to a deficiency of the pancreatic enzymes in the intestine are often conspicuous, but diabetes occurs only when the lesions are far advanced. On the other hand, in chronic interacinar pancreatitis glycosuria or actual diabetes is almost always present, but symptoms of intestinal indigestion may be inconspicuous or wholly absent.

**Symptoms.**—In mild cases of chronic interlobular pancreatitis there are often no definite symptoms, probably because the secretions of the stomach and intestine are capable of acting vicariously. Even in the more severe forms of the disease the symptoms are not characteristic. In many instances, however, there are digestive disturbances with increasing weakness and emaciation, deep-seated pain in the upper part of the abdomen and tenderness. Neither the location of the pain nor its paths of radiation are distinctive. Vomiting is not uncommon, and during the more active exacerbations it may be persistent. Jaundice, due to obstruction of the common bile-duct by calculi or by the enlarged and indurated pancreas, and often intermittent at first, is present at some time in about one-half of the cases. Constipation is the rule, but obstinate diarrhea is sometimes a prominent feature. Glycosuria is occasionally observed. It was present in 6 per cent. of 65 cases of chronic pancreatitis following cholelithiasis treated by Robson[3] and in 7 per cent. of 30 cases treated surgically by Deaver.[4] Salivation (sialorrhea) has been noted in a few instances. Certain changes in the stools are suggestive, but it is noteworthy that they occur only when the reduction of the pancreatic

[1] Deutsch. Arch. f. klin. Med., 1899, lxii.
[2] Amer. Jour. Med. Sci., Aug., 1916.
[3] Brit. Med. Jour., April 23, 1910.
[4] Surg. Clin. of North America, Feb., 1921.

secretion is pronounced and that they may be present also in other lesions of the pancreas, such as tumors, cysts, or calculi, which occlude the ducts, and in rare instances as a congenital anomaly (Garrod and Hurtley,[1] Miller and Perkins[2]). The stools are often pale and voluminous, and show large amounts of fat (steatorrhea) and numerous undigested muscle fibers (azotorrhea). Fatty stools, however, have diagnostic value only when jaundice is absent and when the diet contains no excess of fat, and azotorrhea is suggestive only when it is pronounced, when there is no diarrhea, and when the ingestion of meat has been within the normal range. Especially significant is the predominance of *neutral* fats, indicating failure of enzymic cleavage, and persistence of the cell nuclei after the ingestion of hardened raw meat cubes (Schmidt's nuclei test), gastric juice having no power to digest nuclei. Very direct evidence of deficient pancreatic secretion may sometimes be obtained by examining the gastric contents for pancreatic ferments after an olive oil breakfast has caused a regurgitation of duodenal liquid into the stomach (Boldyreff's method), or, better still, by sampling undiluted duodenal contents obtained by means of the duodenal tube. Much less significance attaches to the absence of trypsin and diastase in the feces, the occurrence of mydriasis following the instillation of adrenalin in the eye (Loewi's test), and a diminished quantity of ethereal sulphates in the urine, and still less to the Cammidge reaction in the urine.[3]

Physical examination is not often helpful. Tenderness in the epigastrium is usually present, and occasionally there is a sense of resistance or an indefinable mass in the region of the pancreas, making the clinical picture closely resemble that of carcinoma. In the cases with jaundice the gall-bladder is, as a rule, distended, which is in contrast with what is found in calculous obstruction of the common gall-duct. In chronic interacinar pancreatitis there is almost always glycosuria, but as the exocrine secretion of the gland is not much affected, the digestive processes are often well maintained.

The **diagnosis** of chronic pancreatitis can rarely be made with certainty, but the existence of the disease may be inferred when disturbances of the pancreatic functions occur in association with lesions of adjacent organs, especially the biliary passages. The chief conditions to be considered in the differential diagnosis are carcinoma of the pancreas, of the bile-ducts, and of the liver, chronic cholecystitis without gall-stones, and perigastric adhesions, the result of peptic ulcer.

**Treatment.**—The treatment of chronic interlobular pancreatitis should aim at the cause, whether this be gall-stones, duodenal ulcer or catarrh, or syphilis. A thorough study of the digestive processes and the adaptation of the diet to existing deficiencies will often lead to improvement. Preparations made from the pancreas are sometimes useful. If after a fair trial of medical treatment the symptoms still persist, the question of draining the biliary tract, and through this outlet also the pancreatic ducts, should be seriously considered. Even when there is no definite evidence of cholelithiasis, cholecystectomy, cholecystostomy, or choledochoduodenostomy may prove effective in arresting the process. The treatment of chronic interacinar pancreatitis is mainly that of diabetes mellitus.

[1] Quart. Jour. Med., 1913, vi, 242.

[2] Quart. Jour. Med., 1920, xiv, 1.

[3] The Cammidge reaction consists in the production of characteristic osazone crystals with the phenylhydrazin reagents after boiling urine, free from protein and preformed sugar, with hydrochloric acid. It depends upon the presence in the urine of a complex carbohydrate, probably dextrin, and the derivation from this of osazone-yielding products by hydrolysis with the acid. Unfortunately it may be positive in health and negative when the pancreas is extensively diseased.

## CARCINOMA OF THE PANCREAS

Carcinoma is the most frequent tumor of the pancreas, but of all carcinomata apparently less than 5 per cent. are in the pancreas, and of these only a small proportion are primary. The disease is more common in males than in females, and usually occurs after the age of 35, although it has been observed in young adults and even in children. An association with pancreatic calculi has only rarely been reported. The growth is commonly of the scirrhous variety, and in the majority of cases begins in the head of the gland. Primary carcinomata frequently extend directly to contiguous structures and give metastasis to adjacent lymph-nodes and the liver. In secondary carcinoma the primary growth is usually situated in the stomach duodenum, the ampulla of Vater, or the biliary ducts.

**Symptoms.**—Digestive disturbances and changes in the feces due to absence of the pancreatic juice are present, as a rule, but are indistinguishable from those usually observed in chronic interlobular pancreatitis. Epigastric pain is rarely wholly absent. In many cases it occurs in paroxysms and radiates toward the back, thus suggesting biliary colic. Jaundice, the result of pressure on the common bile-duct, often occurs; it may develop gradually or suddenly, is persistent and intense, and is usually associated with distention of the gall-bladder. In some instances, but certainly not in the majority, a tumor or ill-defined mass, deep seated and usually fixed, and not rarely transmitting the pulsation of the aorta, becomes palpable at or above the umbilicus. Ascites supervenes in about one-third of the cases. It is usually the result of cancerous peritonitis, but it may be due to compression of the portal vein.

The urine occasionally contains sugar and toward the close of life it may be slightly albuminous. Exceptionally the general nutrition of the patient remains good for a comparatively long time, but as a rule, weakness, emaciation and cachexia develop more quickly and with greater intensity than in other intra-abdominal carcinomata. Symptoms due to compression or invasion of adjacent organs are not uncommon, and may obscure the primary condition. Thus, stagnation of the gastric contents and dilatation of the stomach may result from pressure on the duodenum or pylorus. Complete intestinal obstruction has also been observed. Hematemesis and enterorrhagia sometimes result from invasion of the stomach or duodenum. Ulceration into one or more of the hollow viscera is somewhat frequent.

**Diagnosis.**—In many cases the diagnosis cannot be made with certainty. The exclusion of *chronic pancreatitis* is often especially difficult as it may produce nearly all the phenomena of carcinoma, including a palpable mass in the epigastrium. In favor of carcinoma are early and pronounced emaciation, a large and rapidly growing tumor, the appearance of ascites, and the absence of any symptoms indicating antecedent cholelithiasis. *Gall-stones in the common bile-duct* may also simulate carcinoma of the pancreas very closely. Usually, however, the former is characterized by periodic attacks of chill, fever and increased jaundice, with intervals of fairly good health, and an absence of any enlargement of the gall-bladder. In *carcinoma of the pylorus* the tumor is, as a rule, more freely movable and evidences of gastrectasis and changes in the composition of the gastric juice are more common, while signs of disturbed pancreatic digestion in the intestine are much less common. X-ray examinations may render valuable aid in doubtful cases. Carcinoma of the common bile-duct, of the duodenum or of the ampulla is generally indistinguishable from carcinoma of the head of the pancreas.

The *treatment* is purely palliative, operations, except in some cases to relieve the jaundice, being inadvisable.

## PANCREATIC CALCULI

Pancreatic calculi are rare, less than 100 cases being on record. They occur most frequently between the ages of 30 and 60, and are much more common in men than in women. The etiology of pancreatic lithiasis is not definitely known, but it is likely that the concretions are produced, as in the case of gall-stones, by bacterial infection of the pancreatic ducts; indeed, the condition is not infrequently associated with cholelithiasis. The calculi are commonly found near the duodenal orifice of the pancreatic ducts, but they may be in any part of the gland. As a rule, several calculi are present, and occasionally more than a hundred have been found. They vary in size from sand-like particles incrusting the ducts to masses as large as a walnut, are of a grayish or brownish-gray color, rounded or elongated, and smooth or rough, sometimes being branched like coral. Their chief constituents are calcium phosphate and calcium carbonate with more or less cellular detritus. The most common sequel of pancreatic lithiasis is chronic interstitial pancreatitis, which sometimes reaches an advanced grade. The ducts of the gland are almost invariably dilated, and occasionally true retention-cysts are formed. Fistulous communications with the stomach or duodenum have been reported. Abscess and carcinoma are rare associations.

The **symptoms** are usually vague and only in a few instances have been correctly interpreted. Marked disturbances depend chiefly on the migration of the stones (colic) and secondary changes in or about the pancreas. Pancreatic colic is usually in no way distinguishable from biliary colic. The presence or absence of jaundice is not very significant, as jaundice is often lacking in cholelithiasis and is occasionally present in pancreatic lithiasis. In the latter it may be due to compression of the common bile-duct or to obstruction of the common duodenal orifice. Decisive evidence is afforded by the recovery of the characteristic concretions from the stools, but this is rarely obtainable, probably because the concretions often fail to escape from the ducts or after entering the bowel break up into minute fragments that are not readily recognized. In addition to colic there may also be indications of disturbed pancreatic function, such as indigestion, with bulky fatty stools, and azotorrhea, but these symptoms are not characteristic, as they may also supervene in the later stages of cholelithiasis. Glycosuria and even diabetes are not rare occurrences, the presence of calculi often exciting an intense grade of pancreatic sclerosis. In obscure cases x-ray examinations might aid in the diagnosis, as pancreatic concretions, in contrast with gall-stones, are rich in lime-salts and therefore likely to cast shadows.

**Treatment.**—The treatment of the colic is that recommended in biliary colic (page 514). In the intervals the treatment is essentially that of chronic pancreatitis (page 549). In the event of recurrent attacks of severe pain, operative intervention should be seriously considered even if the diagnosis is not fully established. Calculi have been successfully removed from the duct of Wirsung by Coe, Moynihan, Robson and others.

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## CYSTS OF THE PANCREAS

Under this heading it is customary to consider not only cysts arising within the pancreas itself—*true pancreatic cysts*—but also cystic accumulations in the lesser peritoneal cavity adjacent to the pancreas—*pseudo-pancreatic cysts*. The true cysts include the following: (1) Retention cysts

(pancreatic ranulæ). These depend upon obstruction of the larger pancreatic ducts by calculi, tumors, strictures, etc. (2) Proliferation cysts. These are definite neoplasms (cyst-adenomata). While usually benign, they may undergo malignant transformation. (3) Necrotic cysts. These occasionally occur as sequels of acute hemorrhagic pancreatitis, the necrotic tissue undergoing liquefaction and then becoming surrounded by a cicatricial capsule. (4) Hemorrhagic cysts. These result from the spontaneous rupture of a pancreatic vessel and the subsequent conversion of the blood-clot into a serous cyst. (5) Hydatid cysts. These have so little in common with ordinary cysts that their consideration does not properly belong here.

Pseudo-pancreatic cysts are more common than true pancreatic cysts and consist of collections of serous or sero-sanguinous fluid in the lesser peritoneal sac. They occur more frequently in males than in females and are usually of traumatic origin, a blow or crushing force applied to the upper part of the abdomen leading to extravasation of blood and pancreatic juice into the lesser peritoneal sac and later to inflammation of the wall of the sac. The cyst generally appears in from 10 days to 4 weeks after the trauma. Honigmann[1] in 1905 collected 70 cases.

The fluid of pancreatic and peripancreatic cysts may be watery or viscid, and almost of any color, although it is usually yellowish or brownish from admixture with blood. It is alkaline in reaction, and microscopically contains fat globules, blood-coloring matter, and cell detritus. The enzymes of the pancreas are often present, but this feature is of less diagnostic significance than was formerly supposed, as the fluid in other abdominal cysts sometimes contains similar constituents.

**Symptoms.**—The symptoms vary according to the location, size and character of the cyst. Pain, usually epigastric, but sometimes referred to the back, and disturbances of digestion are the most constant subjective manifestations. Not rarely the pain occurs in paroxysms and is accompanied by vomiting. Steatorrhea, azotorrhea, glycosuria and other evidences of interference with the functional activity of the pancreas are observed in a small proportion of cases. Weakness and emaciation are frequently noted. Jaundice, due to closure of the common bile-duct, sometimes supervenes and occasionally there are symptoms of intestinal obstruction. Ascites or edema of the lower extremities, as a result of pressure on the portal vein or vena cava may also occur. The clue to the diagnosis, however, is the appearance of a smooth rounded tumor in the epigastrium, either in the median line or a little to the left of it. The tumor usually reaches the abdominal wall between the stomach and the colon, but it may be present above the stomach or below the colon. It is often slightly movable and, if superficial, may yield a sense of fluctuation. In cases of traumatic origin the appearance of the tumor is frequently preceded by symptoms of acute pancreatitis. Rupture of the cyst into the peritoneal cavity or intestine sometimes occurs and may be marked by a sudden disappearance of the abdominal swelling. Cysts of other abdominal structures, especially those of the mesentery, omentum, and ovaries, and also distended gall-bladder and hydronephrosis must be considered in the differential diagnosis. The **treatment** is surgical and usually by incision and drainage. In 138 cases the mortality was 11.6 per cent. Aspiration is dangerous and should not be practised, even for diagnostic purposes.

[1] Deutsch. Zeit. f. Chirurg., lxxx, No. 1.

# DISEASES OF THE PERITONEUM

## ACUTE DIFFUSE PERITONITIS

**Etiology.**—Although it is possible to excite acute peritonitis experimentally by introducing chemical agents into the peritoneal cavity, it is generally admitted that clinically the disease is always the result of bacterial infection. Two forms are recognized, the primary and the secondary. The latter is by far the more common. The term *primary peritonitis* is applied to cases in which the infecting organisms have come from some source other than a local lesion adjacent to the peritoneum. Such a primary peritonitis may develop in the course of an infectious process in a distant part of the body, or rarely it may arise as an independent affection. Undoubtedly the microörganisms are usually brought to the peritoneum by the blood or lymph channels, but it is conceivable that in some instances the invasion may occur through the intact intestinal wall or the mouths of healthy Fallopian tubes. Primary peritonitis of hematogenous origin is sometimes observed in the course of general specific infections and also somewhat frequently as an intercurrent or terminal event in chronic diseases that lower the resistance of the tissues, such as cirrhosis of the liver, chronic cardiac and renal disease, cancer, etc. The infection-atrium in such cases is not always discoverable, but it may be an abscess, an ulcer or a wound at any distance from the peritoneum.

*Secondary peritonitis* may follow an abdominal wound or a traumatic injury to the peritoneum or to an abdominal viscus, or it may be due to an infectious process in some organ or part adjacent to the peritoneum, invasion of the latter being effected by actual perforation into the cavity or by simple extension. Among the most important causes of this form of peritonitis may be mentioned appendicitis, peptic, typhoid and amebic ulcers, visceral and other abscesses, intestinal obstruction and infarction, phlegmonous cholecystitis, pyosalpinx and diverticulitis.

**Bacteriology.**—Acute peritonitis is most commonly associated bacteriologically with colon bacilli, streptococci, staphylococci, or pneumococci Occasionally the Bacillus pyocyaneus is encountered. In many cases the infection is mixed. The colon bacillus is found most often in the cases resulting from lesions in the alimentary canal. Streptococci are found in a large proportion of the grave cases accompanied by bacteriemia. Pneumococcus peritonitis is comparatively rare, and is observed chiefly in children. Of 244 cases in children collected by Barling[1] females were affected in 73 per cent. and males in 27 per cent. From their study of pneumococcus peritonitis in children, Annand and Bowen[2] conclude that in about one-third of the cases the disease is secondary to some remote pneumococcus lesion, such as pneumonia, otitis, or sore throat, and in the large majority of the remaining two-thirds the peritoneum is probably infected from the bowel, although the Fallopian tubes must also be considered as possible portals of entry in female patients. In some cases the peritoneum appears to be the only focus of the pneumococcus infection and occasionally primary pneumococcus peritonitis is succeeded by infection of other parts, such as the lung or pleura. General peritonitis from gonococcus infection is rare and occurs chiefly in females, the peritoneum being invaded by way of the Fallopian tubes. In 1907, Goodman[3] collected 75 cases. The disease is usually of a mild type.

[1] Pediatrics, May, 1912.
[2] Lancet, June 9, 1906.
[3] Annals of Surgery, July, 1907.

**Morbid Anatomy and Pathogenesis.**—Infection of the peritoneum, if sufficiently intense, is productive of the various local changes commonly observed in inflammation of other serous membranes and also of more or less profound systemic disturbances, due to the entrance of the bacteria and their toxins into the blood. The anatomic changes depend upon the cause, intensity and stage of the inflammatory process. The earliest change is hyperemia. This is more marked in the visceral than in the parietal layer of the peritoneum, and is especially pronounced, as a rule, near the starting point of the inflammation. Following closely upon the hyperemia there is fibrinous exudation, which may take the form of a dull, finely granular, sticky membrane, glueing together, here and there, adjacent coils of intestine, or, less frequently, of loosely adherent, opaque, yellowish flakes, unevenly distributed over the congested surface. Accompanying the fibrin there is usually more or less fluid exudate, and this may be either serous or purulent. In some instances the exudate becomes sanious or putrid, and occasionally it is charged with gas. The amount of fluid is usually small, but there may be several liters. In diffuse pneumococcus peritonitis the signs of peritoneal irritation are, as a rule, less pronounced than in other forms of the disease, but there is usually an abundant fluid exudation, of a milky white color, and without odor. In gonococcus peritonitis the exudate usually consists of somewhat dry tenacious fibrin.

The organs covered by the peritoneum are always more or less affected. The intestines are distended, the intestinal walls are softened and edematous, and the solid organs to a depth of several millimeters beneath the peritoneum are infiltrated and degenerated.

In cases which end favorably the exudate may be completely absorbed; commonly, however, some fibrin remains in the form of adhesions. Diffuse purulent peritonitis, although almost always fatal, occasionally ends in recovery even without, operation the pus after becoming encysted, or even while it is still free, discharging itself spontaneously into one of the hollow viscera or through the abdominal parietes.

The grave constitutional disturbances of acute diffuse peritonitis are due to septicemia, resulting from the invasion of the blood by pathogenic bacteria and their toxins. As shown by Fowler,[1] Buxton[2] and others, absorption of bacteria occurs almost entirely through the lymphatics of the diaphragm and omentum; hence the greater tendency to recovery in peritonitis localized in the lower portion of the abdomen. Occasionally, owing to an overwhelming infection and a rapid overthrow of the natural defences—phagocytic action of the endothelial and other cells, the bactericidal power of the peritoneal fluid, and the intercepting and destructive functions of the mesenteric lymph-nodes—fatal bacteriemia occurs before any marked changes are produced in the peritoneum (*diffuse septic peritonitis*).

**Symptoms.**—The symptoms vary and are often modified or veiled by those of the primary disease. Severe pain, frequently localized at first to the starting point of the inflammation, but extending later over the entire abdomen, is usually the earliest symptom. It is constant, although aggravated by the slightest movement, and is accompanied by tenderness, sometimes so extreme that even the weight of the bedclothes is almost unbearable. In order to relax the abdominal muscles, the patient usually maintains a dorsal decubitus with the head and shoulders raised, and the knees drawn up and flexed. The facial expression is one of suffering and anxiety.

Physical examination of the abdomen generally reveals marked tympa-

[1] Medical Record, April 14, 1900.
[2] Jour. Med. Research, 1906, xv and 1907, xvi.

nitic distention, with diminution and upward displacement of the hepatic dulness, board-like rigidity of the recti and other abdominal muscles, and later, if the liquid effusion is considerable, dulness on percussion in the most dependent parts. Lividity of the skin, disappearing on pressure, is often observed in severe cases, and is to be ascribed to vasomotor disturbance. Occasionally, friction-sounds, coincident with respiration, may be heard, especially over the liver. Owing to the abdominal tenderness and distention, the respiratory movements are hurried, shallow and thoracic.

Persistent vomiting of bile-stained mucus is fairly constant, and occasionally as the disease advances the vomitus becomes feculent or bloody. Eructations and hiccough are also common. The tongue, at first moist and coated with white fur, may eventually become dry, brown and fissured. Owing to spasm of the intestinal muscles in the earlier stages and to paresis of the bowel in the later stages, there is, as a rule, obstinate constipation. Fever is usually, but not invariably, present, the temperature in most cases ranging between 100° and 103° F. The pulse-rate is increased and toward the end in fatal cases it may rise to 150, 160, or 170 per minute. In the early stages the pulse is small and hard, and in the later stages, weak and thready. The urine is scanty, high colored, and contains an excess of indican and not rarely a trace of albumin. Interference with micturition is not uncommon. Except in fulminating cases, with overwhelming infection, examination of the blood reveals marked polymorphonuclear leucocytosis. Profound systemic depression, shown by pallor and coldness of the surface, clammy sweats, pinched features, huskiness of the voice, and an almost imperceptible pulse, soon supervenes in unfavorable cases and death comes within a few days, sometimes in perforative cases, within twenty-four hours. The mental faculties are often unaffected throughout the disease, but there may be muttering delirium or stupor toward the end.

The peculiar features of *pneumococcus peritonitis in children* are the somewhat stormy onset, the frequent occurrence of herpes, the tendency to diarrhea, and the greater tendency than in other forms of diffuse peritonitis to encapsulation of the exudate (encysted peritonitis). In *diffuse puerperal peritonitis* chills are common, diarrhea is often present instead of constipation, septic processes frequently develop in other parts and the course is, as a rule, rapidly fatal. In *gonococcus peritonitis* the onset is usually stormy, but the temperature is only slightly elevated, there is no pronounced abdominal rigidity, and a decided amelioration of the symptoms frequently occurs on the second or third day. Primary peritonitis occurring in the late stages of wasting diseases (*terminal peritonitis*) often runs an almost latent course.

**Diagnosis.**—The diagnosis of acute peritonitis is usually an easy matter, although difficulties may arise in the early stages of the attack when sharp abdominal pain and vomiting are the chief features. The various forms of *colic* are, as a rule, readily excluded. It may be otherwise, however, with *acute intestinal obstruction*, as this condition often exists with peritonitis in the relation of either cause or effect. Uncomplicated intestinal obstruction may generally be distinguished by the colicky character of the pain, the stercoraceous vomiting, the absolute constipation, and the absence of fever, leucocytosis, tenderness, and rigidity. *Acute pancreatitis* simulates perforative peritonitis very closely. The former should be suspected if the pain and distention are confined to the epigastrium and the collapse is sudden and profound, especially if the history points to cholelithiasis.

The *peritoneal hopalgia* of *hysteria* may be confused with peritonitis, but in the former condition there is usually a suggestive history, other hysterical stigmata are often present, the cutaneous hyperesthesia is excessive, slight

friction of the abdominal wall not rarely exciting as much distress as deep pressure, and, moreover, all general indications of infection are wanting.

In determining the cause of acute peritonitis careful consideration must be given to the previous history of the case and to the initial symptoms of the attack.

**Prognosis.**—Acute diffuse peritonitis is a highly dangerous disease and in the large majority of cases is fatal. An important factor is the degree of toxemia and this is determined largely by the rapidity of the infection, the variety and strain of the inciting agent, and the resistance of the patient. Peritonitis due to streptococci or Bacillus pyocyaneus is especially dangerous. Colon bacilli cause a grave form of peritonitis, but the process is likely to spread less rapidly than when caused by streptococci. Pneumococcus peritonitis and the rare gonococcus form are relatively mild.

**Treatment.**—This is chiefly surgical. Important points in the auxiliary treatment, both before operation and for from 24 to 48 hours afterward, are the maintenance of the semi-erect position of Fowler, in order that the exudate may be kept away from the diaphragm where absorption is most active; the withholding of food and water by the mouth; the avoidance of purgation; the washing out of the stomach to relieve vomiting; and the administration of normal saline solution by continuous proctoclysis (Murphy's method) and also, if necessary, by subcutaneous or intravenous injection. Morphin should be avoided until a decision has been reached in regard to operation, as it masks the symptoms and favors the occurrence of intestinal paresis. Collapse may be treated by the external application of heat and the administration of camphor, epinephrin, strychnin and atropin.

## ACUTE CIRCUMSCRIBED PERITONITIS

Acute circumscribed peritonitis occurs in two forms: sero-fibrinous and suppurative. In almost all cases it is secondary to injury or disease of the abdominal or pelvic viscera. Not rarely it is observed as a residual process in persons who have recovered from acute diffuse peritonitis. The limitation of the inflammation to the region in which it originated is to be ascribed to active peritoneal resistance, to low virulence of the infecting organisms, to slow invasion, or to a combination of these factors. In the *sero-fibrinous form* the clinical picture may be essentially the same as that of the primary condition which produced the peritonitis, although in many cases the occurrence of the latter is made evident by localized pain, tenderness and rigidity. Constitutional symptoms, with the exception of slight fever, are usually absent unless the inflammation is severe or shows a tendency to become diffuse. The process may end in resolution, but very often it results in adhesions, which in turn may lead to various sequelæ, such as functional disturbances of the stomach and intestines, constriction of the pylorus, strangulation of the bowel, etc.

*Circumscribed suppurative peritonitis* presents itself as an abscess (periappendicular, perimetric, subphrenic, etc.), the walls of which are formed partly by inflammatory exudate and partly by agglutinated viscera, the mesentery and omentum, or the parietal peritoneum. The symptoms are those of septic infection—fever, chills, sweats, prostration and leucocytosis—with localized pain, tenderness, muscular rigidity, and, in many cases, a palpable tumor. The purulent collection may be partially absorbed, but more frequently it ruptures into one of the hollow abdominal organs, the

vagina, the general peritoneal cavity, the pleura and lungs or the pericardium, or it discharges externally through the abdominal wall. In other cases it remains intact and death results from general septicemia, from pneumonia, from purulent pleurisy or pericarditis, or from suppurative pylephlebitis.

## SUBPHRENIC ABSCESS

A collection of pus or of pus and gas between the diaphragm and the viscera immediately below it is known as a subphrenic abscess. The most frequent causes of this condition are acute appendicitis, peptic ulcer, and suppuration in the liver. Other causes are abscess of the spleen, pancreas or kidney, carcinoma of the stomach, pyosalpinx, spinal tuberculosis, contusions of the abdominal viscera, and intrathoracic suppuration (empyema, pulmonary abscess, etc.). Probably because the lymph flow through the diaphragm is ascending, intrathoracic suppuration only exceptionally results in a subphrenic abscess, although the latter frequently gives rise to the former.

The purulent collection may be intraperitoneal or extraperitoneal, and may occupy one or several of the suphrenic fossæ. Those on the right side are most often involved through disease of the appendix and liver, and those on the left side through peptic ulcer. Occasionally an abscess resulting from appendicitis is on the left side. In about one-third of the cases the abscess is gaseous.

**Symptoms.**—The onset may be sudden or gradual. Abdominal pain, often accompanied by vomiting in cases due to perforative peritonitis, is, as a rule, the first indication. Symptoms of septic infection—fever, acceleration of the pulse, chills, pallor, and leukocytosis—usually follow. Local signs may be absent, but in many cases there is bulging of the lower ribs or a swelling in the abdomen on one side, with deep-seated tenderness. Litten's diaphragm shadow may be present and not rarely exaggerated flaring of the costal margin and widening of the infracostal angle on inspiration may be observed. Occasionally, enlargement of the superficial veins and edema of the skin may also be noted. If the abscess contains pus only, the note on percussion is dull, if it contains both pus and gas (*subphrenic pyopneumothorax*), there is a tympanitic area at the base of the thorax, changing in outline as the patient changes his position, with other signs of pneumothorax. Thoracic signs indicative of pleurisy or pneumonia are often present. The x-ray yields valuable information. The diaphragm is found to be immobile and projected upward on the affected side. The heart, though sometimes elevated, is rarely displaced laterally as in pleural effusion. Exploratory puncture through the thoracic wall often aids materially in diagnosis. When the needle enters an abscess below the diaphragm the discharge of pus is greater during inspiration and less during expiration, while the reverse is true in the case of empyema. The withdrawal of different fluids at different levels is suggestive, but not pathognomonic, of subphrenic suppuration.

Much difficulty may be experienced in distinguishing between a subphrenic abscess and a purulent collection above the diaphragm. This is especially true because of the frequency with which the two conditions co-exist. In the diagnosis much importance attaches to the history, to the mode of onset, and the x-ray findings. Narrowing of the infracostal angle on inspiration and absence of Litten's phenomenon are in favor of a supradiaphragmatic condition.

Without surgical intervention subphrenic abscesses are almost always fatal, death usually resulting from septicemia or extension of the abscess into the lung, pericardium or, rarely, the peritoneum. Occasionally there is spontaneous recovery, due to rupture of the abscess and discharge of the pus. Of Bernard's[1] 76 cases 64 were treated surgically and in these the mortality was 37.5 per cent.

## CHRONIC DIFFUSE PERITONITIS

In the large majority of cases diffuse peritonitis with a gradual onset and a protracted course is obviously either tuberculous or carcinomatous (for the description of these forms the reader is referred to pages 43 and 560 respectively). In some instances, however, the nature of the underlying condition is obscure, although apparently it is not tuberculous and certainly it is not carcinomatous. Doubtless infection by bacteria of relatively low virulence is an essential factor in every case. Chronic diffuse peritonitis of the peculiar type in question is not uncommon in chronic nephritis, chronic alcoholism and ordinary cirrhosis of the liver. In a few instances it seems to have been due to trauma.

In one group of cases the peritoneum is affected with other serous membranes, such as the pleuræ and pericardium, the condition known as *multiple serositis, Concato's disease,* or *Pick's disease* being produced. Rarely, syphilis may be a factor, and occasionally a diffuse peritonitis, not in itself carcinomatous, may have its point of origin in a small carcinoma of the ovary or some other organ. It is well to remember, too, that many of the apparently non-tuberculosis cases are in reality tuberculous, the bacilli, although not revealed in the exudate by microscopic examination, being demonstrated by animal inoculation when a sufficiently large amount of the fluid is injected.

Anatomically, several forms of the disease are observed. In one form there is much serous exudation, and the peritoneum is opaque and slightly thickened, but adhesions are few or absent (*chronic exudative peritonitis*). In another form the serous effusion is less copious, but there are numerous and firm adhesions, sometimes leading to sacculation of the abdominal contents or converting the omentum or segments of the intestine into a mass that may simulate an abdominal tumor. Occasionally the peritoneum is obliterated (*chronic adhesive peritonitis*). In a third form the peritoneal membrane is the seat of a peculiar overgrowth of fibrous tissue, which undergoes hyaline metamorphosis with the production of gristly plaques or cartilaginous sheets in various places, especially around the liver and spleen. Serous exudation, sometimes copious, is usually present (*chronic proliferative or hyperplastic peritonitis*). The process, generally circumscribed at first, may by degrees extend until it involves large areas of the peritoneum. Not rarely, however, it is confined almost exclusively to the liver, constituting *chronic hyperplastic perihepatitis,* or the "sugar-iced liver" (Zuckergussleber) of Curschmann. In this condition the liver itself, although usually small from compression, is not markedly cirrhotic. In multiple serositis there is a chronic fibrous inflammation, usually hyperplastic, of several serous membranes—peritoneum, pleuræ, and pericardium. In some cases the inflammation of the pleuræ or pericardium may be shown to be primary, and that of the peritoneum secondary, while in other cases the reverse must be assumed.

[1] British Med. Jour., Feb. 22, 1908.

The layers of the pleuræ and pericardium are thickened and often united by adhesions. Not rarely the mediastinal connective tissue is likewise involved. The peritoneum is also thickened, especially around the liver and spleen, and these organs are, as a rule, adherent to the diaphragm and other adjacent structures. A considerable quantity of serous fluid is usually present. General arteriosclerosis and granular kidneys accompanied the chronic perihepatitis in 19 of 22 cases analyzed by Hale White.[1]

The **symptoms** are variable. In some cases the disease is latent and is entirely unsuspected during life. In other cases the symptoms are chiefly those arising from interference with gastrointestinal motility—intermittent colicky pains, dyspepsia, flatulence, and constipation. In a third group of cases there are in addition to the gastrointestinal disturbances signs of abdominal effusion, free or encysted, with, perhaps, palpable tumor-like masses. Occasionally the bowel is caught under a fibrous band and actual strangulation ensues. In the hyperplastic forms the symptoms frequently simulate closely those of hepatic cirrhosis with ascites. Chronic peritonitis should be suspected, however, if there is no alcoholic history, if the spleen is not enlarged, if other signs of portal stasis (hematemesis, melena, etc.) are wanting, and especially if the ascites necessitates repeated tappings, and tends to recur rapidly after tapping. If with such ascites signs of pleurisy or pericarditis are present, or there is a history of a previous attack of pleurisy or pericarditis, it is likely that the case is one of multiple serositis.

## CHRONIC CIRCUMSCRIBED PERITONITIS

Chronic circumscribed peritonitis is usually of the adhesive type, but it may be hyperplastic. A form analogous to chronic hemorrhagic meningitis is occasionally observed in the pelvis, delicate layers of richly vascularized connective tissue developing and becoming the seat of hemorrhagic extravasations and pigmented deposits. Localized adhesive inflammation may occur in any part of the peritoneal cavity, but the areas about the female genital organs, the cecum and appendix, the colonic flexures, the gall-bladder, and the stomach are the most common points of election. The adhesions may be relics of a previous attack of acute peritonitis, or they may be a result of peritonitis which has been chronic from the beginning. External trauma and operative procedures often give rise to them. Pelvic peritonitis in women is an extremely common sequel of gonorrheal endometritis and other inflammatory diseases of the uterus and its appendages. Chronic peritonitis limited to the right iliac region is usually the result of chronic appendicitis, but it may be due to tuberculosis, neoplasms, or even fecal accumulation. Whether the veil-like pericolic membranes described by Jackson are of inflammatory origin or are developmental has not been definitely determined. Peritonitis around the gall-bladder is frequently excited by cholelithiasis. Perigastric adhesions depend, as a rule, upon ulcer or cancer of the stomach but not rarely they may be traced to inflammation originating in the gall-bladder. Partial adhesive perihepatitis and partial adhesive perisplenitis are observed in many forms of chronic disease of the liver and spleen respectively, and less frequently as extensions of inflammatory processes originating in the lungs, pleuræ or pericardium. Finally, chronic circumscribed peritonitis may be dependent upon various lesions of the kidneys, pancreas, urinary bladder, amebic or other ulcerations

[1] Quoted by Rolleston: Dis. of the Liver, 1904, p. 166.

of the bowel, new growths or glandular enlargements in contact with the peritoneum, and hemorrhagic extravasations into the peritoneal cavity.

**Symptoms.**—The disease may exist without clinical manifestations, or it may give rise to a great variety of local disturbances. The latter are usually of mechanical origin and are frequently due to interference with the movements of the abdominal organs. The most constant symptom is pain, which is often peculiar in being aggravated by exertion and relieved by rest and mechanical support. According to the location of the adhesions it may take the form of intestinal colic, or it may mimic that of gastric ulcer or gastric cancer, biliary colic, or chronic appendicitis. Objective signs are frequently wanting, but there may be localized tenderness, and occasionally a tumor-like mass is present, suggestive of carcinoma. The general health of the patient often remains good, although in some cases morbid nervous conditions, such as neurasthenia or hypochondriasis, supervene, and not rarely there are produced serious mechanical complications, such as strangulation of the bowel, volvulus, stenosis of the pylorus, or compression of the common bile-duct.

The **diagnosis** must rest in the main upon the history of some disease with which peritonitis is frequently associated and upon the exclusion of all other lesions. Without recourse to celiotomy mistakes are often unavoidable. Other treatment than surgical, is usually futile and even from this complete success cannot always be guaranteed, as not rarely after operation fresh adhesions develop or the old ones reform. Temporary relief is often afforded by regulation of the diet, rest, and the application of a suitable abdominal supporter.

## PERITONEAL AND RETROPERITONEAL TUMORS

Benign tumors of the peritoneum are rare. Malignant tumors are almost always secondary, although endothelioma occasionally occurs primarily. Secondary carcinoma of the peritoneum is fairly common, being derived by metatasis from growths in the abdominal organs or from more remote structures. Retroperitoneal tumors are frequently primary and may be either malignant or benign. Of 53 cases treated surgically at the Mayo Clinic, 29 of the tumors were malignant, 18 were benign, and 6 were undetermined (Magoun).[1] Primary malignant tumors in the retroperitoneal space are sarcomatous and arise from the lymph-nodes, connective tissue, Wolffian bodies or Müller's ducts. According to Steele,[2] who analyzed 96 cases, primary retroperitoneal sarcoma is usually lobulated, not larger than a man's head, and often cystic.

Of benign retroperitoneal tumors, the most important are the lipomas, which usually arise from the renal region or the iliac fossa. These growths may reach an enormous size (20 to 60 pounds) and are often so soft as to give the impression of fluctuation, hence they have been mistaken in some instances for ascites or ovarian cysts. In 1908 Proust and Treves[3] collected 89 cases from the literature.

**Symptoms.**—*Carcinoma of the peritoneum* usually takes the form of chronic peritonitis with serous effusion. In addition to the usual phenomena of ascites (see p. 562) there may be evidence of a primary growth, enlarge-

[1] Med. Clin. of N. America, Nov., 1919.
[2] Amer. Jour. of Med. Sci., June, 1904.
[3] Rev. de gyn. et de chirurg. abdom., 1908, xii.

ment of the lymph-nodes in the groin or in the neck, more or less abdominal pain, progressive emaciation, and cachexia. In some instances the umbilicus, owing to metastatic invasion, becomes thickened and indurated, and not rarely definite tumors or a cord-like mass consisting of a curled and infiltrated omentum can be felt through the abdominal wall, especially after the fluid has been withdrawn. Hemorrhagic or milky exudates are much more common than in tuberculous peritonitis.

The spontaneous rupture of certain ovarian cysts and even of cysts of the vermiform appendix may give rise to a peculiar painless form of chronic peritonitis (*pseudomyxoma peritonei*), characterized anatomically by marked thickening of the peritoneum, extensive adhesions, the accumulation of large quantities of free or encysted gelatinous matter, and sometimes the occurrence of small papillary elevations throughout the peritoneum (Werth,[1] Merkel,[2] Trotter,[3] Wilson,[4] McCrae and Coplin[5]). Essentially the process is malignant, although its exact nature is somewhat obscure. However, early removal of the primary lesion and thorough cleansing of the peritoneum may effect a cure.

The important evidences of *retroperitoneal sarcoma* are the presence of a deep-seated abdominal tumor, usually immovable, hard at first, but with a tendency to become soft, and giving rise to cachexia and to various pressure symptoms, such as digestive disturbances, pain in the abdomen or legs, constipation, occasionally amounting to intestinal obstruction, interference with micturition, and edema of the extremities. The presence of the colon between the tumor and the anterior abdominal wall (best shown by inflation of the bowel) is characteristic of retroperitoneal growths.

*Retroperitoneal lipomas*, unlike sarcomas, grow slowly, but often attain a great size, are soft or even fluctuating, and are slow in producing pressure symptoms and in affecting the general health.

The **diagnosis** of peritoneal and retroperitoneal tumors is usually difficult and frequently impossible without recourse to an exploratory operation. In secondary malignant growths, except pseudomyxoma peritonei, **treatment** is only palliative. In other cases surgical intervention offers the only hope of cure. In the 96 cases of primary retroperitoneal sarcoma collected by Steele operation was undertaken in 29 with recovery in 11. Of 26 cases of retroperitoneal lipoma treated surgically recovery occurred in 12 (Adami[6]).

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## ASCITES

The accumulation of serous fluid within the peritoneal cavity is known as ascites.[7] It may occur either as a transudation or as an exudation. The chief causes of the condition are: (1) chronic cardiac disease, such as tricuspid insufficiency, mitral stenosis or mitral insufficiency, adherent pericardium, etc.; (2) cirrhosis of the liver, especially atrophic (portal) cirrhosis; (3) chronic renal disease, especially chronic tubular nephritis; (4) chronic peritonitis from various causes, such as tuberculosis, carcinoma, etc.; (5)

[1] Arch. f. Gynäk., 1884, xxiv, S. 100.
[2] Lubarsch u. Ostertag's Ergebnisse, 1903, Abt. 2, S. 965.
[3] Brit. Med. Jour., 1910, i, 687.
[4] Lancet, 1912, ii, 1496.
[5] Amer. Jour. Med. Sci., 1916, cli, No. 4, 491.
[6] Montreal Med. Jour., 1896, xxv, 529.
[7] The word "ascites" is from ἀσκός, "a wineskin."

neoplasms of the various abdominal organs, with or without glandular metastases, particularly ovarian and uterine growths; and (6) anemic and cachectic states, such as occur in pernicious anemia, leukemia, etc. Among the less frequent causes of ascites may be mentioned diseases of the liver other than cirrhosis, causing portal obstruction, such as carcinoma, syphilis, amyloid degeneration, thrombosis of the portal vein, and thrombosis of the hepatic veins; enlargement of the spleen, such as occurs in leukemia and splenic anemia; and obstruction of the thoracic duct from various causes.

In many diseases more than one factor may be concerned in the production of ascites. Thus, in cirrhosis of the liver, chronic peritonitis may play a rôle no less important than that of interference with the portal circulation. The ascites occurring with solid ovarian tumors may be due to compression of the vena cava, to metastatic growths in the liver, or to chronic peritonitis, and that occurring in myeloid leukemia may be the result of the splenic tumor, of the cachexia, of perisplenic peritonitis, or of general leukemic peritonitis.

**Symptoms.**—The abdomen is enlarged and in general uniformly rounded, but with a tendency to bulge in the flanks when the patient lies on his back. Only in encysted ascites is there likely to be marked asymmetry. The maximum abdominal girth is at or slightly above the umbilicus. The parietes are stretched, the skin is shiny and sometimes scarred as in women after frequent pregnancies, the umbilicus is everted and pouched, or after a time, flattened out, and the subcutaneous veins are often distended and prominent. If the fluid is free a distinct wave-like fluctuation may often be felt by placing the hand flat on one side of the abdomen and tapping gently with the fingers on the opposite side. In eliciting this sign, however, it is advisable to have an assistant place his hand edgewise in the median line in order to interrupt any impulses that may be transmitted through the abdominal wall itself. Percussion ordinarily yields a dull note over the most dependent parts of the abdomen where the fluid tends to gravitate, and a tympanitic note over the highest part where the gas-containing intestines tend to float. Only when the intestines are firmly bound down by adhesions is there likely to be dulness in the uppermost part of the abdomen or entire absence of resonance in front. Shifting of the dull and tympanitic areas on change of posture is proof of free fluid in the peritoneal cavity.

Secondary symptoms due to the mechanical effects of the fluid are often present. Thus, there may be dyspnea and disturbance of the cardiac action from upward displacement of the diaphragm, indigestion from interference with gastric motility, oliguria and slight albuminuria from pressure on the renal vessels, and edema of the lower extremities from compression of the inferior vena cava. Occasionally, spontaneous discharge of the fluid occurs through some weak point in the abdominal wall, most frequently at the umbilicus.

Fluid obtained by paracentesis is usually clear, of a yellowish or greenish hue, and alkaline. It has a specific gravity of 1005 to 1020 and contains from 0.2 to 5 per cent. of albumin. Fluid of inflammatory origin usually has a specific gravity above 1015 and contains more than 3 per cent. of albumin. Cytologic studies sometimes yield important clues in diagnosis, a preponderance of lymphocytes pointing to tuberculous infection and an excess of polymorphonuclear leucocytes to subacute inflammation. In simple dropsy from mechanical causes, such as that resulting from hepatic cirrhosis or cardiac disease, the sediment contains, as a rule, but a few isolated endothelial cells. Not rarely, especially in intra-abdominal malignant disease and tuberculous peritonitis, the ascitic fluid is blood-stained.

Occasionally the fluid has an opalescent, milk-like appearance due to the presence of chyle (*chylous ascites*) or the presence of fat derived from degenerated cellular elements or non-fatty matter, probably a lecithin globulin complex (Wallis and Scholberg[1]), which is held in suspension (*pseudochylous ascites*). In true chylous effusions the total solids are usually in excess of 4 per cent., the total protein content is generally more than 3 per cent., the fat content is comparatively high (about 1 per cent.), and the fat is in finely divided form and corresponds to the fat contained in the food. No sharp line, however, can be drawn between chylous and pseudochylous ascites and in some instances no doubt the two conditions co-exist. True chylous ascites is caused by a leak in the thoracic duct or its tributaries, the result of obstruction (new growths, tuberculosis thrombosis of the left subclavian vein, filariasis, etc.) or of external violence. Pseudochylous ascites is usually associated with tuberculous or carcinomatous peritonitis.

**Diagnosis.**—Ovarian cyst, pancreatic cyst, pregnancy with hydramnios, intra-abdominal lipoma, distention of the urinary bladder, and distention of the bowel with fluid feces are conditions that may be mistaken for ascites. A large cyst of the ovary sometimes simulates ascites very closely and the differentiation is rendered more difficult by the not infrequent co-existence of the two conditions. The distinctive features referable to uncomplicated *ovarian cyst* are: The commencement of the enlargement on one side of the abdomen, as shown by the history, an asymmetrical distention with little tendency to bulge in dependent parts, a maximum girth below the umbilicus, an upward or lateral displacement of the umbilicus, indistinct fluctuation, dulness chiefly in front and often more to one side than the other, unequal edema in the legs, and finally immobility, elevation, and perhaps, lateral displacement of the uterus.

The diagnosis of the *cause* of ascites is considered in the descriptions of the various diseases with which the condition is most often associated.

[1] Quart. Jour. of Med., 1910, Part I, and 1911, Part II.

# DISEASES OF THE RESPIRATORY TRACT

## ACUTE CATARRHAL RHINITIS

(Coryza; Acute Nasal Catarrh; Common Cold)

Acute inflammation of the nasal mucous membrane is always endemic in populous districts, and at certain seasons, especially in the autumn and spring, it frequently becomes epidemic. The ordinary form of the disease is undoubtedly infectious and at times contagious. The commonest organisms found in the nasal discharge are Micrococcus catarrhalis, pneumococci, pyogenic cocci, Bacillus influenzæ, and certain diphtheroid organisms, especially the Bacillus segmentosus of Cantley. Kruse[1] and Foster[2] find that the disease is produced by an ultra-microscopic and filterable virus. Bloomfield[3] also concludes that the common cold is due to none of the ordinary bacteria occurring in the nose and throat, although he finds that these organisms are responsible for the complications of the disease. Droplets of secretion projected into the air in sneezing and coughing and dust from dried nasal discharges are apparently the chief sources of infection.

As in similar infections, individual susceptibility plays an important rôle in the etiology of the disease.

Of the predisposing causes, chilling of the body is one of the most important. It probably acts by temporarily checking the protective nasal secretions. Chronic hypertrophic rhinitis renders the individual particularly susceptible. Deficient ventilation in places of public assembly is often responsible for the spread of the disease.

As a secondary condition, acute nasal catarrh occurs in a number of systemic infections, notably measles and influenza, and special forms of the disease result from overdoses of iodids and, when a peculiar susceptibility exists, from the inhalation of the pollen of certain grasses and plants.

**Symptoms.**—The disease is ushered in with chilliness, malaise, a sense of fulness in the head, smarting in the nostrils, and sneezing. Slight fever and its associated symptoms are usually present. The nasal passages are partially or wholly closed by the swelling of the mucous membrane, so that the patient has to breathe through his mouth. For the same reason the voice acquires a nasal tone. The sense of smell is lost or perverted, and the sense of taste is often blunted. At first the nasopharynx is abnormally dry, but soon an abundant, watery acrid discharge appears and as a result the nares and upper lip become more or less irritated. Herpes sometimes follows. The inflammation may extend to the pharynx and cause tickling in the throat and pain on swallowing, or it may enter the larynx and give rise to hoarseness and cough. In some cases it involves the Eustachian tubes and occasions slight deafness; in other cases it passes into the lachrymal ducts and causes redness of the eyes and an overflow of tears. Sometimes the disease spreads to the frontal sinuses and gives rise to pain in the forehead, and occasionally

[1] Münch. med. Woch., 1914, lxi, 1547.
[2] Jour. Amer. Med. Assoc., 1916, lxvi, 1180.
[3] Johns Hopkins Hosp. Bull., 192, xxxii, No. 362.

it invades the maxillary sinuses and produces pain in the cheeks and soreness of the teeth. In two or three days the discharge becomes muco-purulent and more abundant and the symptoms begin to subside. Recovery is usually complete in from one to two weeks. However, suppurative inflammation of the middle ear or of the nasal accessory sinuses, bronchitis and pneumonia are not uncommon sequels.

The **diagnosis** is not difficult. Care must be taken to exclude infections, such as measles and influenza, which often begin with coryza, and also inflammation of the nostrils due to the presence of a foreign body.

**Treatment.**—If the patient is seen at the outset and is willing to remain indoors for twenty four hours, a hot foot-bath with a full dose of Dover's powder, followed in the morning by a saline aperient, often yields good results. Frequently such a combination as the following will afford some relief:

℞. Codeinæ sulphatis..... gr. ii (0.13 gm.)
Ammonii carbonatis..... gr. xxx (2.0 gm.)
Extracti belladonnæ..... gr. i (0.065 gm.)
Pulveris camphoræ..... gr. xv (1.0 gm.)
Acetphenetidini..... gr. xxx (2.0 gm.) M.
Pone in capsulas No. xv.
Sig.—One every three hours.

Cleansing of the nares with warm, well-diluted Dobell's solution usually lessens the local discomfort, especially if it is followed by an oily application as a protective. The following combination may be used:

℞. Mentholis..... gr. iii (0.2 gm.)
Petrolati liquidi..... f℥j (30.0 mils) M.

Inhalations of menthol are also useful. When there are recurrent attacks of acute rhinitis the indications are to procure the best hygienic conditions, to improve the patient's general health, and to remove any local obstruction that may exist in the nasal passages. The use of mixed stock vaccines may also be tried, but the results are frequently disappointing.

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## EPISTAXIS

Hemorrhage from the nasal cavities occurs at all periods of life, but it is most common in the young, particularly at the age of puberty. Certain individuals are especially prone to nose-bleed, and sometimes the disposition to it is hereditary. The blood usually issues from one nostril, not often from both, and as a rule, it comes from the anterior part of the septum. The amount of blood lost varies from a few drops to many ounces. The hemorrhage rarely proves fatal, and in the majority of cases it ceases spontaneously.

Epistaxis results from a variety of conditions, local or general, among which the following are the most important: (1) Traumatism, either from blows or other injuries. In fractures involving the base of the skull hemorrhage from the nose is often free and persistent. (2) Gross lesions of the nares, such as chronic rhinitis, nasal diphtheria, septal erosions or ulcerations, deflections of the septum, and new growths. Osler[1] has described a family form of recurring epistaxis associated with multiple telangiectases of the skin and mucous membranes. (3) Increased blood pressure and changes in the walls of the bloodvessels. Epistaxis is of frequent occurrence in chronic heart

[1] Johns Hopkins Hosp. Bull., 1901, xii, 333 and 1907, xviii, 402.

disease, especially mitral lesions, in chronic nephritis with arterial hypertension, in arteriosclerosis, and in cirrhosis of the liver. (4) General diseases characterized by certain deficiencies in the blood, such as hemophilia, purpura hemorrhagica, scurvy, and severe anemias. In more than one-half of the 334 cases of hemophilia analyzed by Grandidier the chief bleedings were from the nose. (5) At the onset of certain infectious diseases, notably typhoid fever. (6) Exposure to rarefied atmosphere, as in the ascent of high mountains. (7) Very rarely from the suppression of the menstrual flow (vicarious menstruation). In Fricher's case, that of a girl of 19 who had never menstruated, epistaxis occurred at regular intervals and finally proved fatal.

**Treatment.**—In certain conditions nose-bleed may prove beneficial by relieving undue tension in the vascular system. There is no doubt that in diseases of the mitral valves moderate epistaxis at times affords considerable relief; again, it is quite possible that spontaneous nasal hemorrhage sometimes averts cerebral apoplexy in middle-aged persons with high blood pressure. Sometimes epistaxis does not cease spontaneously, but becomes excessive. Under these circumstances active measures must be adopted. The patient should be kept quiet, with the head and shoulders slightly elevated, and should be directed to breathe through the mouth. Ice may be applied over the nose or nape of the neck, and one or both hands held above the head. Injections of cold diluted vinegar or insufflations of tannin or of powdered alum may often be used with advantage. The most efficient local remedy, however, is epinephrin, applied on a cotton tampon (1:1000). Powdered coagulose or coagulen, on a pledget of cotton, is recommended in hemorrhagic diseases. If the blood is found to issue from a small ulcer, the Paquelin cautery (brought to a dull red heat), chromic acid, fused on the end of a probe, or silver nitrate may be applied. If the bleeding resists these measures the nares should be plugged. Internal remedies are not often of service, although calcium lactate, by the mouth, may prove effective in bleeding associated with jaundice and fresh blood serum (30 mils daily), intravenously or subcutaneously, in that due to hemophilia or purpura hemorrhagica. In the after-treatment the indications are to overcome anemia, if this is pronounced, and to remove, if possible, any underlying condition that may be a cause of epistaxis.

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## ACUTE LARYNGITIS

### (Simple Catarrhal Laryngitis)

Acute inflammation of the laryngeal mucous membrane may take the form of (1) simple catarrhal laryngitis, (2) spasmodic laryngitis, (3) pseudomembranous laryngitis.

**Etiology.**—Chilling of the body and overuse of the voice are important predisposing causes of acute laryngitis. The disease is frequently a part of a general catarrh involving successively the nose, pharynx, trachea, and bronchi, and is doubtless of microbic origin. The Micrococcus catarrhalis, influenza bacillus, pneumococci, and streptococci appear to be the organisms most frequently concerned in the process. Sometimes acute laryngitis a local expression or a complication of a general infection, such as measles, influenza, and typhoid fever. Less frequently it is due to the inhalation of

irritating dusts or vapors, the swallowing of very hot liquids or corrosive poisons or the lodgment of a foreign body.

**Symptoms.**—The affection comes on with a sense of tickling, heat or constriction in the throat and a desire to cough. The voice becomes hoarse and soon may be almost completely lost, the patient not being able to speak above a whisper. The cough is short and barking. It is at first dry, but later on it is associated with more or less mucopurulent expectoration. The larynx is sensitive on pressure, and coughing and attempts at phonation are painful. In adults dyspnea is usually absent, unless there is marked edema of the submucous tissue, when it may be intense. A moderate degree of fever is often present, especially toward evening.

*Laryngoscopic examination* reveals redness and swelling of the mucous membrane. The entire larynx may be affected or the inflammation may be confined to certain parts, such as the true and false vocal cords, the arytenoid cartilages, or the interarytenoid space. The inflamed parts are often coated here and there with mucous secretion and not rarely the vocal cords fail to come in close apposition with each other during phonation owing to a slight loss of power in the inflamed intralaryngeal muscles.

Uncomplicated acute laryngitis usually lasts from a week to ten days and terminates in recovery. The diagnosis rarely presents any difficulties.

**Treatment.**—In severe cases the patient should be confined to bed, and the temperature of the room should be kept uniformly at 70° F. The use of the voice should be avoided. A hot foot-bath is sometimes of service. Cold compresses externally often afford much relief. Inhalations of steam impregnated with compound tincture of benzoin or oil of eucalyptus are useful. At the onset it is advisable to administer a mild aperient. Sedative expectorants, such as potassium citrate and ipecac, may be given with paregoric or codein, when the cough is severe.

## SPASMODIC LARYNGITIS

In children between the ages of two and five years laryngitis, even of a mild type, not infrequently gives rise to sudden attacks of dyspnea, especially at night. These attacks, which have been given the name of *false croup* or *spasmodic croup*, are to be ascribed to spasm of the laryngeal muscles. Thus, a child, who has been in apparently good health or who may have been slightly hoarse and feverish for a day or two, is awakened abruptly in the middle of the night with labored efforts at inspiration, huskiness of the voice and a short barking cough. The face is flushed, and, in severe seizures, cyanotic, the expression is anxious, the pulse is accelerated, and the skin is hot. Notwithstanding its threatening aspect, the attack almost invariably ends in complete and spontaneous recovery. In from a few minutes to half an hour the breathing becomes natural, the cough ceases, perspiration appears, and the child again falls to sleep.

Two or three similar attacks may occur in the same night, but on the following day the child seems well or at most presents the evidence of slight laryngeal catarrh. A recurrence of the paroxysms for two or three nights is not unusual.

**Diagnosis.**—Spasmodic croup must be distinguished from pseudomembranous croup (laryngeal diphtheria) and laryngismus stridulus. In *pseudomembranous croup* the symptoms of laryngeal obstruction come on slowly and grow progressively worse, while in spasmodic croup they appear suddenly, usually at night, attain their maximum intensity at once, and are quickly followed by intervals of complete relief. Furthermore, in a large

proportion of all cases of true croup false membrane may be seen on the fauces or tonsils.

*Laryngismus stridulus* is a spasmodic affection of the larynx occurring chiefly in children who present evidences of rickets, tetany or enlarged thymus. The attacks of apnea are brought on usually by emotional stress, are of momentary duration, commonly recur over a period of weeks or months, frequently result in a lapse of consciousness, and are not associated with catarrhal symptoms, such as fever, hoarseness or croupy cough.

**Treatment.**—A sponge wrung out of hot water may be applied over the larynx or the child may be placed in a hot bath. If these simple measures fail an emetic (1 to 2 teaspoonfuls of syrup of ipecac) will usually afford relief. A moist atmosphere tends to prevent a recurrence of the attacks. In the intervals the treatment is that of simple catarrhal laryngitis. A combination of a sedative expectorant, such ipecac or potassium citrate, with an antispasmodic, such as potassium bromid, antipyrin or belladonna, is often useful.

℞. Tincturæ aconiti..... ♏xvi (1.0 mil)
Syrupi ipecacuanhæ..... f℥i (4.0 mils)
Potassii bromidi..... ℥i (4.0 gm.)
Syrupi limonis..... f℥ss (15.0 mils)
Liquoris potassii citratis.....q. s. ad f℥ii (60.0 mils) M.
Sig.—A teaspoonful every 2 or 3 hours for a child of 3 years.

In older children the application of cold compresses to the neck has a favorable effect.

## PSEUDOMEMBRANOUS LARYNGITIS

In the vast majority of cases laryngitis accompanied by the formation of a false membrane is a manifestation of diphtheria and owes its origin to the Klebs-Loeffler bacillus, the infection usually extending downward from the fauces but at times attacking the larynx primarily. Indeed, so rarely is the disease nondiphtheritic that many authors use the terms *pseudomembranous croup* and *true croup* synonymously with *laryngeal diphtheria.* It must be admitted, however, that false membrane may be formed in the larynx, as in the pharynx, through the action of microörganisms other than Klebs-Loeffler bacilli, especially streptococci and pneumococci, or even of intensely irritating vapor or liquids. Seuvre[1] and Menetrier[2] have each reported a case of membranous laryngitis in which virulent pneumococci alone were found. Except by bacteriologic examination there is no way of distinguishing between the two groups of cases. In both the chief symptoms point to gradually increasing laryngeal stenosis and consist of huskiness of the voice, croupy unproductive cough, distressing dyspnea, stridulous respiration, inspiratory recession of the soft parts of the thorax, extreme restlessness, lividity of the face and stupor. The constitutional symptoms are usually not severe. *Owing to the great preponderance of the cases which are unquestionably diphtheritic and the possibility of an error being made in the bacteriologic diagnosis, especially in a single examination, all cases of membranous laryngitis should be regarded and treated as genuine laryngeal diphtheria* (see p. 119).

[1] Rev. mens. des Mal. de l'Enf., 1898, vol. xvi.
[2] Soc. Méd. des Hop. de Paris, Dec. 9, 1904.

## EDEMA OF THE LARYNX

(Edema of the Glottis)

**Etiology.**—*Simple edema of the larynx* is occasionally observed as a part of the general dropsy resulting from chronic cardiac disease or nephritis. In rare instances it also occurs in consequence of pressure on intrathoracic veins by a tumor or aneurysm, in which case the transudation is local. *Inflammatory edema of the larynx* sometimes develops as a complication of acute laryngitis arising from mechanical injury, the inhalation of hot steam, or the ingestion of caustic substances. It occasionally accompanies tuberculous, syphilitic or cancerous ulceration of the larynx. This form of edema may also result from the extension of inflammation from adjacent structures. Thus, it may follow phlegmonous pharyngitis (Ludwig's angina) or severe tonsillitis. It is a rare complication of acute infectious diseases, such as erysipelas, typhoid fever, and smallpox. The edema laryngis which sometimes appears very suddenly in Bright's disease probably also belongs to the category of inflammatory edemas. The larynx is occasionally affected in angioneurotic edema and urticaria. In a case of angioneurotic edema involving the larynx recorded by Morris[1] tracheotomy was performed on three occasions and in a fourth attack the patient succumbed before medical aid could be obtained. In a few instances laryngeal edema has followed the administration of iodids.

**Symptoms.**—The chief symptoms are rapidly increasing dyspnea, especially on inspiration, huskiness of the voice or actual aphonia, and, not infrequently, a loud inspiratory stridor. Sometimes there is more or less ineffectual cough.

The edematous swelling, which usually involves the epiglottis and ary-epiglottic folds, and only rarely the vocal cords or infraglottic tissue, can be recognized with certainty by a laryngoscopic examination, although it may be very difficult to adjust the mirror, owing to the intense dyspnea. Fortunately, the epiglottic swelling can often be seen from the mouth, without the aid of the laryngoscope, simply by depressing the root of the tongue, or can be felt by passing the finger over the parts.

The **prognosis** is grave, especially in acute cases, in which death from suffocation may supervene before medical aid can be procured.

**Treatment.**—Mild attacks sometimes yield to the application of an ice-bag to the neck, the sucking of ice, external depletion by leeches, the use of astringent sprays (epinephrin, alum, tannic acid) and the administration of saline purges. If the symptoms are urgent the edematous parts should be scarified under cocain anesthesia, and if this fails, tracheotomy should be performed at once. Intubation rarely affords relief unless the obstruction is infraglottic.

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## ACUTE CATARRHAL BRONCHITIS

(Acute Tracheobronchitis)

Acute catarrhal inflammation of the bronchial tubes is an extremely common disease. It is widely distributed, but it prevails most extensively in cold, damp climates and in seasons which are marked by sudden changes in the weather. It affects persons of all ages, but it is especially frequent and severe in infancy and old age. Certain individuals show a marked predis-

[1] American Journal of Medical Sciences, Sept., 1905.

position to the disease. Children with rickets and enlarged tonsils are particularly susceptible. Occasionally bronchial catarrh is directly excited by the inhalation of irritating vapors or dusts, but in the vast majority of cases it is of microbic origin. The organisms most commonly found in the secretions are the Micrococcus catarrhalis, streptococcus, staphylococcus and pneumococcus. The influenza bacillus may also be present, even in the absence of the general symptoms of influenza. Mixed infection appears to be the rule. Exposure to cold, fatigue, and sitting in ill-ventilated rooms are important auxiliary factors in infection. Very frequently the disease is consecutive to coryza or pharyngitis.

As a secondary process bronchial catarrh is often met with in the course of general infectious diseases, such as measles, whooping cough, influenza and typhoid fever.

**Morbid Anatomy.**—The trachea and the larger bronchi of both lungs are the parts usually affected. The mucous membrane is reddened, swollen, and bathed with mucus or mucopus. Microscopic examination reveals distention of the capillaries, enlargement of the mucus glands, degeneration and desquamation of the epithelium, and more or less leucocytic infiltration of the mucosa and submucosa.

**Symptoms.**—The disease is usually ushered in with chilliness, lassitude and general muscular soreness. Fever is slight, the temperature rarely reaching 102° F. Cough is constantly present, but varies much in severity in different cases. At the outset it is harsh and dry and accompanied by a sense of soreness or by actual pain behind the sternum. Very violent cough may give rise to general thoracic pain and headache. Expectoration soon follows, the sputum at first being scanty and composed of viscid, glairy mucus. After four or five days the discharge becomes mucopurulent and at the same time more plentiful. With this change in the expectoration the cough loses its distressing character and the general symptoms rapidly abate. Dyspnea is almost always absent if the inflammation is confined to the large and medium sized tubes.

In many cases physical examination reveals nothing abnormal. Very commonly, however, the ear detects a few scattered râles over both sides of the chest, which may be musical (sibilant and sonorous) or mucous (fine and coarse) according as the secretion is scanty and viscid or is abundant and fluid. Not rarely dry and moist râles alternate with one another.

**Diagnosis.**—Bronchitis must be distinguished from *bronchopneumonia*. When physical examination reveals fine subcrepitant râles and localized areas of dulness the diagnosis of pneumonia may be made with considerable certainty. Even in the absence of these signs, however, pneumonia may be suspected in cases in which dyspnea, cyanosis and pronounced indisposition are added to symptoms of acute bronchitis. *Whooping-cough* in the first stage may easily be mistaken for acute bronchitis, but soon the spasmodic character of the cough, injection of the eyes, puffiness of the face, cyanosis, vomiting and inspiratory whoop lead to a correct diagnosis. A bronchitis that for no obvious reason resists treatment for six weeks or more, particularly if it occurs in adolescence or early adult life, should always excite a suspicion of *tuberculosis*. If with the cough there is also a persistent afternoon rise of temperature the evidence in favor of tuberculosis is almost complete. Bronchitis with the physical signs confined to one side or to the apical regions points strongly to tuberculosis. Finally, the possibility of a bronchial catarrh being *symptomatic of influenza, measles or typhoid fever* and not an independent disease will often have to be considered.

**Prognosis and Course.**—In healthy adults the prognosis is favorable,

recovery usually occurring in from one to three weeks. Attacks that are due to the influenza bacillus or the streptococcus are, as a rule, the most refractory. In children, the aged, and persons enfeebled by previous illness, the prognosis must be guarded, since in these subjects the catarrhal process shows a marked tendency to spread into the smaller tubes and alveoli, and to produce bronchopneumonia. In persons suffering from chronic heart disease, chronic kidney disease, or gout, the disease may gradually develop into chronic bronchitis.

**Treatment.**—If the patient be weak or old he should be confined to his room or even to bed. It is advisable to keep the atmosphere of the room moist and at a temperature not above 70° F. In the early stage a hot foot-bath at bed time, with a Dover's powder and a hot drink, often appears to influence favorably the course of the disease. The food should be simple and readily digestible, and the bowels should be kept regularly open by the aid of mild aperients. Counterirritation to the chest in the form of sinapisms or stupes is very beneficial. In the first stage, when there is little secretion, sedative expectorants—ipecac, potassium citrate, and tartar emetic—are indicated. It is often necessary to add a sedative, such as opium or one of its derivatives (codein, ⅛–⅙ grain—0.008–0.01 gm.) to allay the distressing cough. A combination such as the following will be found useful:

℞. Potassii citratis..... ʒiii (12.0 gm.)
Vini ipecacuanhæ..... fʒiiss (9.5 mils)
Tincturæ opii camphoratæ..... fʒiii (11.0 mils)
Succi limonis..... fʒss (15.0 mils)
Syrupi.....q. s. fʒvi (175.0 mils) M.
Sig.—A tablespoonful every three or four hours.

When the secretion is more abundant, but still tenacious, ammonium chlorid is usually effective. It may be prescribed with brown mixture or syrup of squill. Balsamic expectorants—terpin hydrate, terebene, oil of eucalyptus, oil of santal and tar—are frequently of service in persistent attacks. Guaiacol carbonate (5 grains—0.3 gm. every three hours) is a valuable remedy when the exudation is purulent and abundant. Such combinations as the following often prove efficacious:

℞. Ammonii. chloridi..... ʒiss (6.0 gm.)
Terpini hydratis..... ʒiss (6.0 gm.)
Codeinæ sulphatis..... gr. iii (0.2 gm.) M.
Pone in capsulas No. xxx.
Sig.—One or two every three hours.

℞. Terebeni..... fʒiss (6 .omils)
Guaiacolis carbonatis..... ʒiss (6.0 gm.)
Codeinæ sulphatis..... gr. iss (0.16 gm.) M.
Pone in capsulas No. xxiv.
Sig.—One every two or three hours.

Inhalations of medicated steam are useful when the cough is excessive. For young children the "croup kettle" is most convenient, but for adults the simplest plan consists in breathing deeply the warm vapor arising from the surface of boiling water. For the purpose a small amount of compound tincture of benzoin, eucalyptol or creosote may be dropped into a wide-mouthed jar half full of boiling water, and the vapor conducted to the mouth through a cone made of stiff paper or a folded towel.

In the aged and infirm alcoholic stimulants are sometimes required. Such tonics as cod-liver oil, iodid of iron, quinin and arsenic are useful during convalescence from severe and prolonged attacks. Much benefit is also obtained from a suitable change of climate.

## CHRONIC BRONCHITIS

**Etiology.**—Chronic bronchitis may follow repeated attacks of acute bronchitis or it may develop gradually as a result of the continued inhalation of irritating dusts or vapors. In the large majority of cases, however, it occurs as a secondary process in the course of other chronic affections of the respiratory tract, chronic cardiac disease, chronic nephritis, or gout. Lord[1] reports that of 161 cases, in which during life there were persistent cough, expectoration and râles, not one was found at necropsy to justify the clinical diagnosis of simple chronic bronchitis. Cardiac insufficiency was the important underlying condition in 103; pulmonary tuberculosis, in 31; non-tuberculous pulmonary infection, in 15; malignant disease of the lung, in 5; bronchial asthma, in 6; and syphilis of the trachea and bronchi, in 1.

Chronic bronchitis is especially prevalent in cold, damp climates, and is almost always more severe in winter. Frequently, the symptoms abate in summer and regularly recur as the weather becomes cold. The disease is most common in old persons.

**Morbid Anatomy.**—In some cases the entire mucous membrane is thickened, partly from an infiltration of round cells and partly from an overgrowth of the fixed connective tissue elements. The mucous glands are enlarged and the epithelium is often replaced by columnar or polygonal cells. In other cases the changes are essentially atrophic. The mucous membrane is pale, all the tunics are thin, the glands and vessels are compressed, and the epithelium is desquamated.

Pulmonary emphysema and dilatation of the bronchi (bronchiectasis) are constantly found in long-standing cases.

**Symptoms.**—Cough and expectoration are the chief symptoms. Dyspnea on exertion may also be present. When severe it is usually due to some associated condition, such as emphysema, asthma or cardiac insufficiency. The cough is variable. It is often paroxysmal, and is frequently more troublesome at night than during the day. It is much influenced also by season, becoming especially severe with the approach of cold, damp weather. The sputum is as variable as the cough; commonly, however, it is abundant and mucopurulent. Febrile symptoms are absent and in many cases the general health of the patient is not seriously impaired.

**Physical Signs.**—In uncomplicated cases inspection, palpation and percussion are negative. Auscultation may also be negative, but more freqently it yields a variable numbers of râles, which are musical (sonorous or sibilant) or mucous (coarse or fine) according to the consistency of the secretion and the size of the tubes affected.

The co-existence of emphysema or asthma gives rise top ronounced dyspnea and to additional physical signs. If emphysema is well developed the chest is enlarged and rigid, the respiratory excursions are slight, the percussion note is hyper-resonant, and the expiratory sounds are feeble and prolonged. If asthma is present, the expiration is prolonged and wheezy, dry râles predominate over moist râles, and the sputum contains the characteristic spiral formations of Curschmann and numerous eosinophilic cells.

**Varieties.**—Several special forms of chronic bronchitis may be distinguished according to the quantity and character of the sputum. In *bronchorrhea* the secretion is very profuse, sometimes exceeding a pint a day. As a rule the sputum is opaque and purulent, but occasionally it is thin, transparent and frothy, like a mixture of white of egg and water. Purulent

[1] Lord, F. T.: Diseases of the Bronchi, Lungs and Pleura, 1915, p. 95.

bronchorrhea is usually, though not invariably, associated with bronchiectasis. Cases of serous bronchorrhea are frequently marked by violent paroxysms of cough and asthma-like attacks of dyspnea. The term *fetid bronchitis* is applied to the rare cases of chronic bronchial catarrh in which the secretions undergo putrid decomposition. The expectoration is copious, of a grayish-green color, and usually thin. It has an extremely fetid odor. On standing it forms into layers: frothy mucus on top, turbid serum in the middle, and thick pus at the bottom. The sediment frequently contains yellowish-white masses known as Dittrich's plugs. These plugs vary in size from that of a pin-head to that of a pea, and when squeezed emit an extremely unpleasant odor. Microscopically, they consist of disintegrated pus cells, clumps of bacteria and crystals of fatty acids. Sputum very closely resembling that of fetid bronchitis may also occur in bronchiectasis, perforating empyema, abscess and gangrene of the lung, and tuberculosis, if there are cavities with stagnating contents. In abscess and gangrene, however, the sputum usually contains elastic fibers and in tuberculosis both elastic fibers and tubercle bacilli. Fetid bronchitis as a condition apart from bronchiectasis is extremely rare, and the latter cannot be excluded with certainty.

*Dry catarrh* is a very intractable form of chronic bronchitis in which there is distressing cough but little or no expectoration. It is seen most frequently in old persons in association with emphysema and asthma.

**Complications.**—*Pulmonary emphysema* develops sooner or later in every case. It may eventually lead to *dilatation of the heart and general venous congestion*. *Bronchiectasis* is also a common sequel. In fetid bronchitis *lobular pneumonia* sometimes supervenes and leads to *gangrene of the lung*. Fetid bronchitis is also an occasional cause of *cerebral abscess*.

**Diagnosis.**—The diagnosis of chronic bronchitis presents no special difficulties. A thorough general examination is always necessary, however, to determine whether the disease is primary or secondary.

**Prognosis.**—Under favorable conditions the disease may be fairly well borne for many years. Except in the early stages, however, it is scarcely susceptible of complete recovery.

**Treatment.**—To meet with any measure of success, treatment must be directed largely toward the prevention of recurrent attacks, and the removal, if possible, of the underlying cause. Indiscriminate routine treatment is to be rigidly avoided. Change of climate, especially in winter, is most beneficial, and should be urged if the circumstances of the patient will permit. If there is much bronchial secretion a dry, warm climate, such as that of New Mexico or Southern California, in this country, and that of Egypt or the Riviera abroad, is generally to be recommended, whereas if there be little expectoration, a moist, warm climate, such as that of Florida, the West Indies, Madeira, Pau, or Algiers is preferable. If patients are unable to avail themselves of the benefits to be derived from a suitable climate, they should remain indoors as much as possible in bad weather, and take every precaution against exposure. Flannel should at all times be worn next the skin, the feet should be kept perfectly dry, and the night-air should be avoided.

The diet should be simple but nutritious. In many cases alcohol in some form acts beneficially.

Underlying chronic diseases should always receive appropriate treatment. If cardiac insufficiency is present, digitalis or strychnin may be required. If there is anemia with general malnutrition, such remedies as iron, arsenic, and cod-liver oil may be given with advantage. If gout is a factor, benefit may be expected from the administration of potassium iodid and alkalies. If renal inadequacy is co-existent, the diet must be very care-

fully supervised, and such measures adopted as will promote the functional activity of the various emunctories.

The *special remedies* most generally useful are the expectorants of a balsamic character, such as terpin hydrate, terebene, oil of eucalyptus, myrtol, and oil of santal. Tar is another remedy of value. It may be used in substance made into pills, or in the form of tar-water or the wine of tar. When the sputum is heavy and purulent, no drug usually acts so well as creosote or the carbonate of guaiacol. Potassium iodid is of service in some cases. It may be tried tentatively when the expectoration is very scanty and viscid, or when there is evidence of a gouty diathesis. If cough is excessive mild anodynes, such as codein or heroin, may be used from time to time to keep it in subjection. Alkalies (sodium bicarbonate, aromatic spirit of ammonia), with or without a few minims of the spirit of chloroform, taken in hot water before rising, will often lessen morning cough and facilitate expectoration.

Benefit is often derived from such combinations as the following:

℞. Terebeni..... f℥i–f℥iss (4.0–6.0 mils)
Olei eucalypti..... āā
Codeinæ sulphatis..... gr. ii–iv (0.13–0.25 gm.) M.
Misce et pone in capsulas No. xxiv.
Sig.—One after each meal and at bed time.

℞. Terpini hydratis..... ℥i (4.0 gm.)
Guaiacol carbonatis..... ℥ii (8.0 gm.)
Strychninæ sulphatis..... gr. ss (0.03 gm.)
Codeinæ sulphatis..... gr. ii (0.13 gm.) M.
Misce et pone in capsulas No. xxiv.
Sig.—One capsule three or four times a day.

Syrup of squill often acts remarkably well in acute exacerbations, especially if the concomitant emphysema is pronounced and the right ventricle is embarrassed. It combines the properties of an expectorant with those of a cardiac stimulant. Ammonium chlorid is an excellent adjuvant.

*Inhalations* are sometimes very efficacious, the most suitable remedies for this method of treatment being terebene, eucalyptol, oil of Scotch fir, creosote, compound tincture of benzoin, and spirit of chloroform. Inhalations of compressed air may prove useful, especially in emphysematous subjects. *Intratracheal injections* have been employed with good results in some cases. From ½ to 1 dram (mils 2–4) of a 1 per cent. solution of guaiacol or of a 2 per cent. solution of menthol in olive oil may be injected between the vocal cords into the trachea once a day, a syringe with a long curved nozzle being used for the purpose.

Occasionally, good results are obtained from the use of autogenous *vaccines* in conjunction with other appropriate measures.

## FIBRINOUS OR PLASTIC BRONCHITIS

Fibrinous or plastic bronchitis is a rare affection characterized by paroxysmal attacks of dyspnea and cough ending with the expectoration of fibrinous casts of limited portions of the bronchial tree. The disease is to be strictly differentiated from true bronchial diphtheria.

**Etiology.**—Fibrinous bronchitis is most common in early adult life and attacks men somewhat more frequently than women. It may occur as a primary condition without antecedent illness, or it may develop in the course

of pulmonary tuberculosis, of chronic heart disease with congestion of the lungs, or of asthma. In a few instances it has occurred in association with pulmonary edema after thoracentesis. In a case reported by Finckle[1] it accompanied actinomycosis of the lung. Finally, there is an *acute form*, which usually comes on during or after some acute infection, as pneumonia, typhoid fever, or measles, but which has been observed also as a result of the inhalation of acrid fumes. Of 98 cases analyzed by Bettmann,[2] 27 were cases of chronic primary fibrinous bronchitis, 14 were associated with tuberculosis, 10 were associated with heart disease, 5 were associated with asthma, 4 followed thoracentesis, and 15 were acute.

**Symptoms.**—In addition to the symptoms of bronchial catarrh, there are periodic attacks of dyspnea and cough ending with the expectoration of characteristic casts. Occasionally, neither dyspnea nor cough is very marked. Fever is sometimes present and in acute cases there may also be chills. The expectoration of the casts is rarely accompanied by more or less severe hemoptysis. During the intervals, which in chronic cases may extend over weeks or months, the patient is comparatively comfortable. The casts are usually expelled as round, flesh-like masses mixed with mucus or muco-pus. When unfolded in water they appear as grayish-white arborescent moulds of a portion of the bronchial tree. The main stem may be as thick as a bronchus of the second or third order, and the whole length of the cast may reach 10 or 15 centimeters. The larger branches are usually hollow. Microscopically, the casts consist of concentric laminæ of fibrillated material immeshed in which are leucocytes and alveolar epithelial cells. Charcot-Leyden crystals, eosinophilic cells and Curschmann's spirals have also been found, but chiefly in the cases related to asthma. Chemically, the casts are composed of fibrin and mucin in varying proportions. As a rule the physical signs are those of ordinary bronchitis. In some cases auscultation reveals an absence of breath sounds over the region of the occluded bronchi, and in other cases very coarse clicking or flapping sounds, which are probably produced by the vibration of partly detached casts.

The **diagnosis** of fibrinous bronchitis is not usually difficult. Care must be taken, however, to exclude true bronchial diphtheria and the rare cases of hemoptysis in which blood casts are expectorated. The **prognosis** of the acute form should be guarded, as death not infrequently results from suffocation. It is exceptional for acute cases to become chronic. Uncomplicated chronic cases may last for years. Kisch's case lasted over twenty-five years.

**Treatment** is not very satisfactory. The general management should be that of simple bronchitis. Inhalations of lime-water appear to be beneficial. Emetics sometimes aid in the expulsion of loose casts. In a case reported by Christian subcutaneous injections of epinephrin temporarily relieved the dyspnea. Potassium iodid seems to have been of service in a few of the chronic cases.

## BRONCHIECTASIS

**Varieties.**—Dilatation of the bronchial tubes may be *cylindrical* or *saccular*. In the cylindrical form the tubes in one or more lobes of the lung are uniformly enlarged in caliber for a variable distance, occasionally as far as their finest ramifications. In the saccular form a circumscribed portion

[1] Beitr. z. klin. Chir., vol. xli, No. 3.
[2] Amer. Jour. of Med. Sci., Feb., 1902.

of a tube is distended into a pouch varying in size from that of a pea to that of a hen's egg, or even larger. Saccular dilatations may occur singly or in large numbers. Not rarely both forms of bronchiectasis are found in the same case. Cylindrical dilatations occur most frequently in the larger bronchi and in those of medium size, while saccular dilatations affect chiefly the smaller tubes. In non-tuberculous cases the lesions are most commonly bilateral and in the lower lobes. Tuberculous bronchiectasis, on the other hand, affects the upper portion of the lung more frequently than the lower, and in a large percentage of cases, probably the majority, it is unilateral.

**Pathogenesis and Morbid Anatomy.**—Dilatation of the bronchi is virtually always a secondary process. It may be the sequel of (1) chronic bronchitis; (2) bronchial obstruction from impaction of a foreign body or compression by an aneurysm or tumor; (3) chronic pulmonary tuberculosis; (4) fibrosis of the lung, the result of pneumokoniosis, unresolved pneumonia, pulmonary syphilis, or chronic adhesive pleurisy. How important a part influenza of the bronchitic type may play in the etiology of bronchiectasis has been demonstrated by the investigations of Leichtenstern, Osler, Boggs, and others. An acute form of the disease involving the bronchioles (bronchiolectasis) is sometimes met with, especially in children, as a result of whooping-cough, measles or other acute infections involving the bronchi. Finally, rare cases have been reported by Grawitz, Stoerk and other in which diffuse bronchiectasis has occurred as a congenital defect.

The chief factors concerned in the development of the disease seem to be: (*a*) Weakening of the bronchial wall by inflammatory processes; (*b*) increased air-pressure in the bronchi from coughing or from the unequal distribution of air, such as occurs when a large bronchus is partially obstructed or a portion of the lung is impervious; and (*c*) pressure of stagnating secretions. Corrigan advanced the opinion that the bronchial wall might also yield to traction from without by contracting connective tissue, but this view has not been universally accepted. It may be that the bronchiectasis occurring in cirrhotic conditions of the lung is due, at least in part, to distortion of the bronchi and unequal distribution of air (Ewart).

The walls of dilated bronchi are always more or less changed. Sometimes they are much thickened from infiltration of the mucosa and hypertrophy of the connective tissue; in advanced cases, however, they are often quite thin owing to atrophy of the muscular and elastic fibers and even of the cartilages. Ulceration is occasionally observed. Large areas are usually lined with flat cells devoid of cilia. The secretion is purulent and in many cases intensely fetid. The pulmonary tissue adjacent to the dilatations is almost invariably cirrhotic, while the peripheral portions of the lung are emphysematous. The pleural membranes are frequently thickened and adherent. Dilatation of the heart, especially of the right ventricle, is not uncommon in long-standing cases.

**Symptoms.**—In many cases the symptoms and physical signs do not differ from those of chronic bronchitis or the pulmonary disease with which the bronchiectasis is associated and the condition remains unsuspected. In other cases, however, the disease may be suspected from the character of the cough and expectoration. The cough frequently occurs in paroxysms at intervals of several hours, and is followed by the discharge of very large quantities of sputum. It is often induced by a change of posture and is likely to be especially severe in the morning. The sputum is mostly purulent, but thin, and on standing shows a tendency to separate into three layers: discolored froth on the top, turbid mucus in the middle and thick granular matter at the bottom. Microscopically, it shows pus cells, fatty crystals,

numerous bacteria, and in some cases hematoidin, but no elastic fibers. Frequently, especially in basal bronchiectasis, the sputum has an intensely fetid odor. The breath, too, may be so foul that the patient becomes an object of aversion. Hemoptysis may occur even in the absence of tuberculosis. It was noted in 17 of 24 cases analyzed by Osler.

In advanced cases dyspnea and cyanosis are usually present, but these symptoms are to be ascribed rather to the concomitant fibrosis and emphysema than to the bronchiectasis itself. The finger-tips and toes are often clubbed and the nails incurved, as in pulmonary tuberculosis and congenital cardiac disease, and not rarely the nose is bulbous. Fever of a hectic type occasionally supervenes and in this case the condition may closely resemble pulmonary tuberculosis. Unless the disease is of the saccular variety and is well developed, the physical signs are indefinite or are those of the dominant co-existing condition, such as tuberculosis, emphysema or fibrosis of the lung. Large sacs usually present the signs of pulmonary cavities—tympanitic resonance, amphoric breathing, metallic consonating râles, and pectoriloquy. The "veiled puff"—a peculiar sound occurring at the end of inspiration and suggesting a puff of air entering a small cavity situated just beneath the ear —is sometimes heard. The roentgen ray is not usually helpful except in the case of aneurysm or a foreign body.

**Diagnosis.**—The diagnosis of cylindrical bronchiectasis cannot often be made with certainty. The saccular form is frequently confused with tuberculosis and abscess of the lung. The fact that tuberculosis and bronchiectasis often co-exist makes the differential diagnosis more difficult. In favor of *non-tuberculous bronchiectasis* are absence of marked constitutional symptoms over a long period, despite the signs of advanced pulmonary disease, extreme clubbing of the fingers, clear pulmonary apices with exclusive lower lobe involvement, and negative findings for tubercle bacilli in the sputum after careful and repeated examinations, including guinea-pig inoculation. Bronchiectasis involving the upper lobes alone is tuberculous in the large majority of cases.

*Pulmonary abscess* is usually much more rapid in onset and characterized by more pronounced constitutional symptoms than bronchiectasis. The presence of elastic tissue in the sputum is in favor of abscess, but its absence is not proof of bronchiectasis.

All cases of bronchiectasis of the lower lobes, especially in children, should be subjected to an x-ray examination, owing to the frequency of which a foreign body in the lungs is responsible for the disease.

**Prognosis and Terminations.**—Bronchiectasis is virtually a permanent condition, except possibly in certain acute cases of slight degree following the specific fevers. As regards length of days, the prognosis is fairly good. Death, unless caused by intercurrent disease, usually results from cardiac insufficiency, septic bronchopneumonia with gangrene of the lung, general septicemia, or hemoptysis. Pericarditis with effusion may also occur. Abscess of the brain is not very uncommon. It was present in more than 11 per cent. of the 72 cases of bronchiectasis analyzed by King.[1] Abscess of the spinal cord has been noted in a few instances (Nothnagel, Chiari).

**Treatment.**—Treatment is unsatisfactory. Careful attention must be given to all the circumstances of the patient's life. An abundance of fresh air, nutritious food, and the use of tonics are of prime importance. Change of residence to a dry, warm, equable climate is often beneficial, but, of course, it is not always feasible.

Stimulant expectorants, especially terebene, oil of eucalyptus, creosote

[1] Scot. Med. and Surg. Jour., June, 1904.

and carbonate of guaiacol, may be tried. Inhalations of creosote, phenol, oil of turpentine, etc. from an oronasal mask or a nebulizer operated by compressed air lessen somewhat the fetid odor of the breath. Intratracheal injections have been used with some success. A combination of menthol (10 parts), guaiacol (2 parts) and olive oil (88 parts) may be used for the purpose, ½ to 1 dram (2.0–4.0 mils) being injected once a day. A valuable adjuvant to medicinal treatment consists in having the patient assume for ten minutes or longer, two or three times a day, postures that will facilitate evacuation of the accumulated secretion. The inverted position, with the body flexed at the waist over the foot of the bed, often accomplishes the purpose in basal bronchiectasis. Compression of the lung by the introduction of nitrogen gas into the pleural sac has been tried, but with little success. If a single large cavity can be definitely located operative intervention may be considered. Excision of the diseased portion of the lung is the only surgical measure that is likely to prove curative, but the mortality from this operation is high.

## BRONCHIAL ASTHMA

**Definition.**—Bronchial asthma is an affection characterized by paroxysmal attacks of dyspnea, in which the chest is distended to its fullest extent, the vesicular murmur is obscured by loud musical râles, and the sputum contains characteristic spiral-like masses of mucus and many eosinophilic cells.

**Pathogenesis.**—Of the many theories that have been advanced to explain the symptoms of the disease, the one attributing them to tonic spasm of the muscle in the smaller bronchi has secured the most general recognition. That contraction of the bronchial muscle is capable of producing the chief phenomena of the attack has been demonstrated experimentally (C. J. B. Williams, Brodie and Dixon, Gerlach, Meltzer). The abrupt onset and equally abrupt ending of the paroxysms in many cases, and the favorable effect of such remedies as atropin and epinephrin also support the view that the disease is essentially spasmodic in its nature.

In addition to the bronchial spasm it is probable that some organic change takes place in the mucous membrane of the bronchioles, otherwise it would be difficult to account for the peculiar exudate which usually appears towards the close of the attack. According to one view the bronchial mucous membrane is intensely congested and swollen, as the result of vasomotor changes (Weber, Störk), and according to another view it is the seat of a true exudative catarrh (Curschmann).

While the exact nature of the process is still somewhat obscure, it is now generally recognized that asthma is usually, if not invariably, an anaphylactic manifestation, or allergic condition, due to some specific foreign protein to which the patient has become sensitized. It has been shown that asthmatic paroxysms in certain cases may be precipitated by the inhalation, subcutaneous injection, or ingestion of the offending protein, and that the nature of the latter may be determined beforehand by cutaneous and ophthalmic tests based on the fact that the cells may react to the protein involved when it is applied to them directly. The abnormal sensitiveness may be inborn, but more frequently it is acquired. The foreign protein may be one contained in plant pollen, animal emanations, food or bacteria. Of animals

concerned in producing anaphylactic manifestation the horse (dandruff and serum protein) ranks first in importance, and the cat (hair) second. Why some persons and not others become sensitized to foreign proteins, and whether factors other than anaphylaxis may be operative in some cases of asthma are questions that at present cannot be answered.

**Etiology.**—Asthma may develop at any period of life from infancy to old age. Children and young adults, however, are especially susceptible. Males are affected twice as frequently as females. Hereditary influence is a factor of some importance and many instances are on record of the transmission of the disease from generation to generation. Not rarely asthma is closely related etiologically to a focus of infection in the nares or accessory parts, the tonsils, the bronchi or perhaps, some structure outside of the respiratory tract. In a few instances the disease has occurred only with pregnancy.

Walker[1] has shown that when asthma develops during the first year of life, it is usually due to milk; that when it appears first during the second year it is usually caused by eggs, or cereals, although it may be due to bacteria; that when it has its onset in childhood after the second year it may be the consequence of food, infection of the upper air-passages (bacteria), animal emanations or pollen; and that when it begins in adult life, especially after the fortieth year, it is almost always excited by bacteria (staphylococci, streptococci, diphtheroid organisms, etc.), and usually manifests itself first as a bronchitis. Throughout childhood, between the ages of two and twelve, the frequency of food as a factor gradually decreases and the frequency of bacteria as a factor gradually increases. Unfortunately in many instances the patient is sensitized to more than one protein.

A seasonal influence is frequently noted. Asthma that occurs only during the summer months and disappears regularly with the first frost is usually excited by pollen (see p. 582), while the type that occurs only in the winter and spring months is usually of bacterial origin.

Patients with bronchial asthma frequently associate their attacks with some exciting cause, such as a sudden change of temperature, the prevalence of particular winds, a damp atmosphere, indigestion, and emotional excitement.

**Symptoms.**—The paroxysms may come on suddenly and without warning, or they may be preceded for a longer or shorter time by certain premonitory symptoms, such as chilliness, languor, depression of spirits, or flatulent distention of the stomach. In many cases the asthmatic phenomena are preceded by the symptoms of bronchial catarrh. The attacks proper usually begin at night, but they may begin at any hour of the day. The patient is seized with intense dyspnea and a feeling of impending suffocation, which compel him to sit upright in bed or to assume a standing position. The face is anxious, sometimes livid; the eyes are prominent, and the skin is covered with cool perspiration. Speech, except in monosyllables, may be impossible. The breathing, especially expiration, is labored and often accompanied by loud wheezing. Inspiration is short and jerky, expiration much prolonged. The number of respirations, however, is not increased. The stomach is frequently disordered, and vomiting is not a rare attendant. The pulse is small and accelerated. The urine is high colored and sometimes deposits a copious sediment of urates. Cough, with more or less expectoration, usually supervenes towards the close of the attack. The expectoration may be viscid or watery. In either case it

[1] Med. Clin. of North Amer., Jan., 1918.

contains large numbers of the spirals of Curschmann, which are quite characteristic of asthma. These bodies are visible to the naked eye, but they are better studied with a pocket lens. They are formed in the smaller bronchi, and consist of threads of mucus twisted into spirals. Most of them also contain a central strand which is more strongly refractive than the outside coil. When highly magnified the spirals are found also to contain numerous eosinophilic cells and the crystals described by Charcot and Leyden. These crystals are colorless, elongated double pyramids. They are not peculiar to asthma, but appear to bear some relation to the presence of eosinophilic cells, being found also in leukemic blood and in stools surrounding animal parasites.

Examination of the blood during the paroxysms usually reveals a considerable increase in the eosinophiles, a proportion of from 10 to 15 per cent. not being unusual.

**Physical Signs.**—As the dyspnea of asthma is essentially expiratory, the chest is found to be abnormally distended, with the upper ribs elevated, and the diaphragm depressed. Notwithstanding the vigorous contraction of the auxiliary muscles of respiration, the chest does not expand but merely moves up and down. The percussion note is normal or hyperresonant. On auscultation the vesicular murmur is found to be obscured or wholly replaced by sibilant and sonorous râles of varying quality and intensity. With subsidence of the attack large and small bubbling râles usually make their appearance. Fluoroscopic examination at the height of the attack reveals immobility of the lungs with fixation and depression of the diaphragm.

The attack usually lasts from a few hours to several days, but it may continue with remissions or even brief intermissions for many weeks. In some cases recovery from the asthmatic phenomena is rapid and complete, in others the patient suffers for a longer or shorter time from slight dyspnea, cough and expectoration. The intervals between the attacks vary in duration from a few weeks to many months. Usually as the disease progresses the attacks become more frequent and prolonged, but less severe.

**Associations.**—In some cases asthma is accompanied by other anaphylactic manifestations, such as urticaria, angioneurotic edema, or eczema. In long-standing cases some degree of pulmonary emphysema is invariably present, and in many instances there is also a concomitant bronchial catarrh.

**Diagnosis.**—Asthma is not likely to be mistaken for any other disease. The *dyspnea of chronic heart and chronic kidney* disease is sometimes paroxysmal, but its origin is usually announced by other symptoms and signs. Moreover, it is not especially expiratory, nor is it ordinarily attended with musical râles and wheezing, with hyperresonance on percussion, with expectoration of Curschmann's spirals or with eosinophilia.

The dyspnea dependent upon *obstruction of the upper air passages* (aneurysm, croup, edema of the larynx, etc.) is essentially inspiratory, and is often accompanied by a peculiar stridor. In so-called *hysterical asthma* the rate of breathing is much accelerated, expiration is not prolonged, and dry râles are absent.

In determining the cause of asthma the age of onset, the period of the year in which the seizures occur, and any associated conditions that may be present must all be carefully considered. As already stated, onset in the first few months of life suggests sensitization to milk and onset after middle life suggests sensitization to bacterial proteins. Summer asthma is usually excited by pollen. A history of antecedent bronchitis points to a bacterial origin. The coexistence of eczema suggests food anaphylaxis and so also does the regular occurrence of digestive disturbances at the time of the

asthmatic attacks. In many cases the type of sensitization can be accurately determined by the skin test. This is positive if a minute quantity of a solution of the protein produces a definite urticarial wheal when it is rubbed into a superficial abrasion or is injected into the superficial epithelial layers. Preparations of various proteins are on the market. According to Walker the majority of sensitive patients with bronchial asthma are sensitive to the proteins of horse dandruff, staphylococcus pyogenes (aureus or albus), wheat and other cereal flours, cat hair and egg. A few patients are sensitive to the protein of milk, feathers, chicken meat, beef, potato, and wool. Sensitization to bacteria is not always revealed by cutaneous tests, and certain cases of asthma do not appear to be in the anaphylactic group.

**Prognosis.**—Asthmatic seizures very rarely, if ever, prove fatal. Permanent recovery sometimes occurs upon removal of the primary cause, but far more frequently treatment affords only partial relief, and the liability to the attacks continues through life. As the disease advances, pulmonary emphysema invariably develops, and then dyspnea may become a more or less constant feature. Eventually dilatation of the heart may supervene as a result of the emphysema and be the cause of death.

**Treatment.**—The cause must be sought for and removed if possible. Patients who are sensitized to particular food proteins often remain free from attacks so long as the offending foods are kept out the diet. Desensitization by subcutaneous injections of the particular proteins is not often successful. Asthmatics who are sensitive to the proteins of horse dandruff and cat hair are not rarely relieved for months at a time by subcutaneous injections of these proteins, and asthmatics who are sensitive to the proteins of staphylococci may be benefited or even cured by vaccine treatment.

Vaccines of the predominant organisms occurring in the sputum are sometimes effective also in asthma resulting from bronchitis. The radical removal of foci of infection, wherever located, is indicated and may afford relief, especially in conjunction with treatment by autogenous vaccines. Removal of obstructions in the nose is sometimes curative, although in the large majority of cases the asthma returns in the course of time. In the case of horse asthmatics, it must be borne in mind that the subcutaneous injection of horse-serum, such as diphtheria antitoxin, may result in a violent or even fatal reaction, unless the patient is first desensitized by frequently repeated and gradually increasing doses. Although it is often impossible to meet fully the causal indication, much can be done to lessen the frequency and severity of the paroxysms. The diet should consist of plain, readily digestible food. The evening meal especially should be light. Vicissitudes of temperature must be carefully guarded against and flannel always worn next to the skin. In poorly nourished subjects tonics do much good. Change of residence sometimes proves of service, but the choice of locality must be determined largely by the personal experiences of the patient. Many sufferers do better in the smoky air of cities than in the country. Asthmatics with moist catarrh usually do well in a dry, warm climate, while those with dry catarrh generally derive more benefit from an atmosphere that is somewhat humid. Among empiric remedies potassium iodid holds the first place especially when the asthma is accompanied by chronic bronchial catarrh. To be effective, the drug must be given in doses of from 5–20 grains three times a day for long periods. Tincture of belladonna (3 to 5 minims thrice daily) is sometimes a useful adjuvant to the iodid. Arsenic is well worth trying when the iodids fail. Grindelia robusta may be of service if there is much catarrh. Strychnin is of value in cases associated with emphysema. Occasionally the prolonged administration

of bromids, by allaying the nervous erethism, seems to increase the interval between the attacks.

*The Attack.*—The most suitable remedy for a particular case can only be determined by trial. Some patients derive great benefit from the fumes of ignited stramonium or belladonna leaves or paper which has been impregnated with potassium nitrate. These agents may be burnt in the patient's room or smoked in a pipe or in the form of cigarets. Occasionally tobacco proves efficacious. Marked alleviation of the paroxysm is sometimes obtained from the inhalation of ethyl iodid (10–20 min.). In some cases the attacks yield to a few whiffs of chloroform, although as a rule the effect of the drug is only temporary. The most reliable remedy in the large majority of cases is epinephrin (adrenalin) hydrochlorid in doses of 15 minims (1.0 mil) subcutaneously. The good effect may last at first two or three hours, but tolerance to the drug is gradually established and eventually it may fail to afford relief. In other cases benefit may be derived from the administration of belladonna, bromids, lobelia, or quebracho by the mouth. Strong hot coffee is occasionally efficacious. If the attacks are accompanied by bronchial catarrh a combination such as the following may be of service:

℞. Sodii bromidi..... ℥iiss (10.0 gm.)
Tincturæ belladonnæ..... f℥iss (10.0 mils)
Tincturæ lobeliæ..... f℥iii (11.0 mils)
Fluidextracti grindeliæ..... f℥ss (15.0 mils)
Aquæ menthæ piperitæ.....q. s. ad f℥iv (120.0 mils) M.
Sig.—A dessertspoonful in water every three hours.

Few attacks of asthma will resist the action of morphin or heroin hypodermically, but the greatest caution must be exercised in using these drugs lest a habit be established. Atropin is often of service and may be given alone or with morphin. The application of sinapisms or of dry cups to the chest sometimes has a good effect.

## POLINOSIS

**(Hay-Fever; Hay-Asthma)**

**Definition.**—An anaphylactic condition occurring during certain seasons of the year, characterized by catarrhal inflammation of the conjunctivæ and upper respiratory tract, and in some cases by asthmatic phenomena, and excited by a protein of plant pollen to which the individual is sensitized.

**Etiology.**—The disease is common in the United States and in England, but is comparatively rare on the continent of Europe. It occurs only in regions in which plants rich in pollen flourish and only when these plants have reached the flowering stage. In this country it is present chiefly in the late spring and early autumn months, although the time of its appearance varies, of course, with the climate. The spring form begins in the middle of May and lasts until the middle of July; the autumn form begins in the middle of August and lasts until October or the first heavy frost. An hereditary tendency to the disease is sometimes noted and persons of a neurotic temperament seem to be especially susceptible. Polinosis usually begins in childhood or early adult life, and is rarely acquired after forty. Obstructive lesions of the nose, such as a deflected septum, hypertrophic rhinitis, polyps, etc., predispose to it by favoring the lodgment and retention of the pollen.

The early (vernal) form of hay-fever is usually caused by the pollen of grasses—timothy, red top, orchard grass, rye, etc., while the late (autumnal) form is in the Northern, Eastern and Southern states is due chiefly to pollens of the ragweeds (*Ambrosiaceæ*) or goldenrod and in the Pacific and Rocky Mountain states to pollens of the wormwoods (artemisias). As a result of multiple sensitization, which is by no means uncommon, or of concurrent bacterial infection an attack of pollen asthma is sometimes prolonged for several months.

**Symptoms.**—The disease usually begins abruptly with itching in the nose and throat, a sense of fulness in the frontal region, and repeated attacks of sneezing. Symptoms of coryza—nasal occlusion, copious watery secretion, blunting of the sense of smell, and tumefaction of the nares—soon develop. The conjunctivæ usually share in the irritation and as a result itching of the eyelids, suffusion of the eyes, lacrimation and photophobia, are added to the patient's discomfort. In severe cases the catarrh extends to the bronchi and there is distressing cough. Not rarely, typical asthmatic attacks make their appearance at the height of the disease. The general health is more or less affected, and many patients suffer greatly from headache, mental depression, lassitude, insommia, anorexia, and indigestion.

**Prognosis.**—Pollen catarrh does not shorten life, and not infrequently the severity of its seizures lessens as age advances, but complete cure is not often observed.

**Treatment.**—The cutting of the weeds in the vicinity of the patient's residence often affords much relief. In New Orleans the vernal type of hay fever is said to have been decreased more than 50 per cent. in one season by the enforcement of weed-cutting ordinances. Nasal abnormalities which favor a concentration of pollen in the nostrils should be corrected Desensitization by means of specific pollen solutions yields good results in a fairly large percentage of cases. The best method is to begin the treatment at least three months ahead of the season of pollination and not to continue it through the season unless the prophylaxis fails. Only the pollen to which the patient reacts by conjunctival or cutaneous test (see p. 581), should be used for a vaccine. The injections should be given at intervals of not less than 3 or 4 days, the dose being gradually increased from the strongest dilution which fails to produce a positive cutaneous test to the strongest dilution (1:100) which gives a positive test. Maver,[1] of the hay-fever clinic at Bellevue Medical College, reports good results from weekly injections throughout the year. If the treatment is carried out during the season considerable caution must be exercised owing to the danger of precipitating an anaphylactic attack. The highest dilution should be given at first and the succeeding doses very slowly increased.

In the majority of cases removal to a region in which the disease does not prevail offers a sure means of avoiding the attacks or of obtaining complete relief if the symptoms have already appeared. Among the localities most frequently resorted to by residents of the Eastern and Middle states may be mentioned the White Mountains, the Adirondacks, and the lake districts of Maine and Canada. Many Americans escape their attacks by travelling in Europe. Owing to individual peculiarities a region that is well suited for one patient often brings no relief to another. A sea voyage affords complete immunity.

For patients who are unable to leave home a strict regimen, a daily tepid bath with friction of the skin, and the avoidance of dust, smoke and direct sunlight tend to make the hay-fever season more tolerable. Tonics, espe-

[1] Jour. Amer. Med. Assoc., April 3, 1920.

cially quinin, arsenic, and strychnin, are frequently useful. A warm alkaline spray or an oil spray is often efficacious. A spray of epinephrin (adrenalin) solution (1:10,000) usually affords temporary relief, but when the effect of the drug wears off the discomfort is likely to be greater than it was before the treatment was used. Cocain should be avoided because of the great danger of establishing a habit. Boric acid washes usually relieve temporarily the itching of the eyes.

## FOREIGN BODIES IN THE AIR PASSAGES

The aspiration of a foreign body into the air passages is relatively common. In 1917 Chevalier Jackson[1] reported a series of 590 cases, 81.6 per cent. of which were in children under 15 years of age. Laryngeal and tracheal obstruction is comparatively rare. If complete, it may cause death by asphyxia in a few minutes. Usually the foreign body passes through the trachea and is arrested in a bronchus, the right one, owing to its larger size and more nearly vertical course, being involved in more than three-fourths of the cases. Among the many objects that have been reported as having lodged in the air passages may be mentioned pins, safety-pins, tacks, screws, collar-buttons, seeds, especially peanuts, fragments of food, pebbles, and artificial dental plates. The body is usually aspirated from the mouth during a sudden deep inspiration, such as may accompany laughing or coughing. It is a remarkable fact that in some instances no history of the accident can be obtained.

Not rarely the foreign body is expelled spontaneously at an early period or after the lapse of many weeks, months, or years. If it remains in the bronchus it may cause bronchopneumonia, abscess formation, bronchiectasis localized fibrosis, or collapse of the affected portion of the lung. Pus is almost always formed below the foreign body, and may be retained, may escape by exciting ulceration or sloughing of the tissues, or may be aspirated into adjacent bronchi or even into bronchi of the unaffected lung.

**Symptoms.**—The immediate effects of a foreign body in a bronchus usually consist of a sense of choking, spasmodic cough, dyspnea, cyanosis, hoarseness, inspiratory wheezing, and bloody expectoration. These symptoms often disappear in from a few minutes to several hours, but are likely to recur at intervals. In some instances the patient experiences no discomfort whatever at the time of the accident.

After a variable period of latency secondary manifestations appear, the most constant being cough, with abundant mucopurulent sputum, remittent fever, sweats, and emaciation. If the process is acute, ordinary bronchopneumonia is usually suspected, if chronic, pulmonary tuberculosis or bronchiectasis.

**The physical signs** vary in different cases and at intervals in the same case. If a large bronchus is completely obstructed the expansion on the affected side is decreased, the percussion note is dull, and the breath sounds are absent. Incomplete but persistent obstruction of a large bronchus may give rise to diminished expansion, dulness on percussion and harsh breathing with râles of varying character. If the foreign body acts as a ball-valve and allows air to enter but not to escape, the percussion note, as a result of overdistention of the lung, may be tympanitic. In other cases the physical signs may be those of pulmonary abscess, bronchiectasis or empyema. Not

[1] Trans. of Sect. on Laryng., Otol. and Rhinol., 1917.

uncommonly there are signs of a generalized bronchitis on the side opposite to the one in which the bronchus obstructed. In children peanut obstruction almost invariably produces an acute, bilateral, purulent bronchitis with wheezing respiration and a great variety of râles. In many cases of bronchial obstruction by a foreign body when the ear of the examiner is placed close to the open mouth of the patient during forced and prolonged expiration a sound resembling the wheezing of an asthmatic person, but drier, (asthmatoid wheeze) is detected (Chevalier Jackson[1]). In from 75 to 85 per cent. of the cases the foreign body is shown by the x-ray. The tracheobronchoscope is also a valuable aid to diagnosis, especially when the foreign body is one that is pervious to the x-ray, but the instrument should be employed only by an operator fully trained in its use.

**Treatment.**—The foreign body can often be extracted by the aid of the tracheobronchoscope. If this direct method fails recourse must be had to ordinary tracheotomy, low tracheotomy or bronchotomy.

## CONGESTION OF THE LUNGS

**Active congestion of the lungs** may result from violent muscular exertion or may be caused by a sudden ascent into a rarefied atmosphere. It may be due to the inhalation of hot or cold air or irritating gases. It marks the first stage of pneumonia and is the concomitant of all inflammatory diseases of the lungs. Woillez described in considerable detail an idiopathic acute congestion of the lung, but this condition is probably nothing more than an abortive form of croupous pneumonia, as Carrière[2] found pneumococci in 9 out of 14 cases.

**Passive congestion of the lungs** results from some direct impediment to the return of blood through the pulmonary veins to the left auricle. The chief cause is cardiac disease, especially lesions of the mitral orifice and weakness of the left ventricle from fatty or fibroid changes. It may be induced also by compression of the pulmonary veins by intrathoracic tumors.

The lungs are dark red in color, heavier than normal and often somewhat edematous. In long standing cases they acquire a brownish-red color and become dense and relatively dry (*brown induration*). In this condition microscopic examination reveals dilatation and elongation of the pulmonary capillaries, overgrowth of the connective tissue and elastica, and infiltration of the alveolar epithelium with granular pigment, a product of the disintegration of free red corpuscles.

**Hypostatic congestion** is the term used to designate a form of passive congestion of the lungs which is prone to develop whenever the body is retained in a recumbent position for a long time and the action of the heart is feeble. It is very common in prolonged infectious diseases, such as typhoid fever, in all affections of the brain attended with coma, and in old persons who from any cause are compelled to lie in bed for weeks. The dependent parts of the lung are dark purple in color, boggy to the touch, and heavy. When cut and pressed they discharge a large amount of bloody serum. Infection very frequently supervenes, transforming the process into *hypostatic pneumonia*. In this condition the parts affected are completely devoid of air and sink in water.

**Symptoms.**—Active congestion of the lungs does not always give rise to distinctive symptoms. As an expression of ephemeral pneumonia, however,

[1] Amer. Jour. Med. Sci., 1918, clvi, No. 5.
[2] Presse méd., Jan. 26, 1898.

it is usually manifested by a chill, moderate fever, pain in the side, acceleration of the respiration and pulse, slight cough, feeble breath sounds and crepitant râles.

Passive congestion of the lungs in most cases is masked by the symptoms of the primary disease and is therefore readily overlooked. As a rule the diagnosis must be based solely upon the objective findings. Over the dependent parts of the lung the percussion note is dull, the respiratory murmur is feeble and there are fine, crackling râles. Dyspnea is frequently observed, but it is dependent in part upon the underlying disease. Cough may be entirely absent, although it is often a conspicuous symptom in the congestion resulting from chronic heart disease. In such cases, too, the sputa usually contain numerous pigmented epithelial cells—the heart-failure cells (*Herzfehlerzellen*) of German writers. These cells are somewhat characteristic of brown induration of the lungs, but not pathognomonic, as they may also be found in the sputum of pulmonary infarction.

The **treatment** of active congestion of the lungs is that of the first stage of pneumonia. The treatment of passive congestion is mainly that of the underlying affection. The application of dry or wet cups to the chest often affords relief. In congestion from heart disease venesection is indicated when the symptoms are urgent. Saline and mercurial aperients are also of service. In hypostatic congestion, in addition to cupping and the free use of stimulants (strychnin, caffein, ammonia, camphor), frequent change of posture is sometimes advantageous.

## BRONCHOPNEUMONIA

**(Lobular Pneumonia; Catarrhal Pneumonia; Capillary Bronchitis)**

**Definition.**—Bronchopneumonia is an inflammation of the terminal bronchioles and the contiguous vesicular tissue, usually affecting disseminated groups of lobules rather than an entire lobe of the lung, and excited by various species of bacteria.

**Etiology.**—The disease is especially common in children during the first three years of life, although it is not infrequent in old persons. Unlike lobar pneumonia, it does not usually attack vigorous individuals at the prime of life. By far the greatest number of cases occur in debilitated, ill nourished subjects. Bad hygienic surroundings and inappropriate nourishment are important predisposing factors. Children suffering from rickets or diarrhea are particularly prone to it. In homes and hospitals for infants the disease is very prevalent and fatal; thus Bovaird[1] found it in 40 per cent. of 500 autopsies at the New York Foundling Hospital. Season exerts a decided influence, the number of cases increasing considerably during the cold and changeable weather of winter and spring.

Bronchopneumonia may occur as a primary disease or as a secondary process in the course of some other affection. The primary form is comparatively uncommon and is observed chiefly in young children as a consequence of exposure to cold. The secondary form may be conveniently divided into the following classes:

1. Cases occurring in the course of the specific fevers, especially those which are accompanied by catarrh of the bronchial mucous membrane, such as measles, whooping-cough, diphtheria, scarlet fever and influenza. Of

[1] Med. News, April 30, 1904.

these diseases measles and whooping cough are easily first in importance. Less frequently bronchopneumonia follows typhoid fever, erysipelas, or cerebrospinal fever.

2. Cases occurring as a sequel of simple bronchitis. Bronchopneumonia from this cause is very common in infants and in many cases it supervenes so quickly upon the bronchitic process that it might with propriety be called primary.

3. Cases occurring in the course of various chronic affections, such as chronic nephritis, diabetes and cardiovascular disease. This form is met with chiefly in old persons, although it is not rare in children. It is usually a terminal event.

4. Cases of so-called aspiration or deglutition pneumonia. This form of the disease results from the aspiration of irritating secretions, septic material, or particles of food into the smaller bronchi. Such an accident is liable to occur whenever the sensibility of the larynx is benumbed, as in apoplexy, uremia, or bulbar paralysis. Cancer of the throat and operations on the upper air passages also favor its occurrence. Many cases of post-operative or ether pneumonia are doubtless examples of aspiration pneumonia. In pulmonary tuberculosis a pneumonitis of this kind is not infrequently excited by a backward flow of the infectious material in the bronchial tubes. In the newborn bronchopneumonia is sometimes caused by the aspiration of secretions from the birth canal. Finally, the pneumonias which follow hemoptysis, the inhalation of irritating gases and submersion also belong in this category.

5. Cases occurring as a result of metastasis in the course of various focal septic infections. In this form the lesions are usually produced by emboli laden with bacteria and, in consequence, are prone to develop into abscesses.

**Bacteriology.**—Although the immediate cause of bronchopneumonia is some pathogenic microörganism, the disease, in distinction from lobar pneumonia, may result from infection by various sorts of bacteria. In the majority of cases more than one microörganism is present. The pneumococcus is found in more than one-half of the cases, sometimes in pure culture, but usually in association with other bacteria. Type IV is the one most frequently present in children. The Streptococcus hæmolyticus is found next in order of frequency, and then the Staphylococcus aureus and albus. In some instances the Bacillus influenzæ, Bacillus pneumoniæ of Friedländer, Micrococcus catarrhalis, non-hemolytic streptococcus, Bacillus diphtheriæ or Bacillus typhosus is found alone or in various combinations. The bronchopneumonias which develop in the course of the specific fevers are usually the result of a secondary infection, although in some cases, especially in diphtheria and influenza, they may be caused by the organism of the primary disease.

**Morbid Anatomy.**—As a rule, both lungs are involved and contain a varying number of patches which are firm to the touch and do not crepitate. These indurated foci are either areas of inflammatory consolidation or of atelectasis. The pneumonic patches project slightly above the surface and present a reddish, or in the later stages, a grayish appearance. The pleura over them is usually covered with a thin layer of fibrin and in consequence is rough and lusterless. On section the inflamed lobules stand out prominently. They are moist and smooth or, if the exudate contains some fibrin, faintly granular. Occasionally minute foci of suppuration are seen throughout the inflamed area. Close examination may also reveal in some of the affected lobules a central bronchiole containing yellow muco-pus, although frequently many of the solidified areas are not visibly peribronchial. However, in the

form of pneumonia which the Streptococcus hæmolyticus frequently produces and which MacCallum has termed *interstitial bronchopneumonia*, because of the extensive infiltration of the alveolar walls about the bronchioles and of the interlobular septa with mononuclear wandering cells, and the tendency of the exudate to undergo organization at an early period, the solidified areas are distinctly peribronchial and appear as small, firm, reddish or yellowish gray nodules, which project above the cut surface like miliary tubercles.

The collapsed patches owe their origin to complete obstruction of the bronchioles and are generally most abundant in the neighborhood of the inflamed areas. Unlike the latter, they have a cyanotic color and are depressed below the general surface. The pleura over them is either normal or the seat of ecchymosis. The patches are usually small and lobular, but exceptionally they involve a large part of a lobe. Some of them are partially pneumonic, owing to the entrance of microörganisms from the bronchioles or adjacent lobules.

Emphysema, with more or less congestion, is frequently found in the neighborhood of the affected portions, and the peribronchial lymph-nodes are usually swollen and hyperemic.

Variations in the process are not rarely observed. In some cases there is very little consolidation, inflammation of the bronchioles being the chief feature. In other instances the infiltration is very extensive and involves whole lobes rather than isolated lobules. In such cases it may be very difficult to exclude genuine lobar pneumonia, especially if, as sometimes happens, the vesicles contain much fibrin and the cut surface presents a granular appearance. When the affected lobe is closely examined, however, it will usually be found that the consolidation is not perfectly uniform, but is interspersed with small areas of tissue that are merely congested. These pseudolobar forms are very commonly associated with the pneumococcus, and may be regarded as being on the borderland between true lobar pneumonia and bronchopneumonia.

In aspiration pneumonia the inflammatory process is very intense and often ends in suppuration or gangrene.

*Microscopically*, the terminal bronchioles are dilated and filled with detached epithelial cells and leucocytes. The walls of the bronchioles and the alveolar septa are swollen and infiltrated with round cells. The capillaries, both of the bronchial walls and septa, are distended. The alveoli contain desquamated epithelial cells, leucocytes, red blood corpuscles, and mononuclear wandering cells in varying proportions. As a rule, fibrin is absent or present only in small amount. In many of the milder cases the epithelial cells predominate, but in the more severe forms of the disease the exudate may consist chiefly of polymorphonuclear leucocytes and red corpuscles. In interstitial bronchopneumonia the important features are the great infiltration of the bronchial and alveolar walls with mononuclear wandering cells and the early transformation of the exudate into connective tissue.

In contrast with lobar pneumonia are the distribution of the lesions through the lungs in patches, the comparatively small amount of fibrin in the alveolar exudate, the participation of the bronchial and alveolar walls in the inflammatory process, and the tendency of the exudate in the bronchial and alveolar walls, at least in many cases, to become organized into soft vascular fibrous tissue.

**Symptoms.**—The symptoms of the *primary form*, which is seen chiefly in infants, more or less closely resemble those of lobar pneumonia. The onset

is often sudden, with vomiting or, less frequently, a convulsion. The temperature rises rapidly to 103°, 104° or 105° F. and may be continuously high. The respiration and pulse are accelerated, the former often out of proportion to the latter. Dyspnea is marked, cyanosis is almost constantly present, and nervous symptoms, consisting of restlessness, insomnia, delirium and jactitation, are conspicuous and may dominate the clinical picture. There may be frequent cough or none at all.

Compared with the severity of the symptoms the physical signs are often poorly developed. In some cases there are numerous râles of various sorts throughout the chest, in other cases fine râles may be heard over a small area or areas, and in other cases still patches of consolidation, yielding slight dulness on percussion, feeble or loud bronchovesicular or bronchial breathing, and bronchophony, may be found, especially over the bases posteriorly.

The outlook is more favorable in primary bronchopneumonia than in the secondary form of the disease. When recovery occurs the disease usually terminates in from 10 days to 2 weeks, the temperature falling by lysis or more rarely, by crisis.

In the *secondary form* the symptoms are less definite, and are often masked by those of the primary disease. In the infectious fevers a change for the worse in the general condition, an increase in the temperature, an exacerbation of the cough, acceleration of the respirations, and a decided disturbance in the pulse-respiration ratio are often the only phenomena to signalize the onset of pneumonia. After the disease is well established signs of deficient oxidation of the blood usually arise. These include dyspnea, restlessness, cyanosis, and sometimes somnolence. The temperature is, as a rule, moderately high and of a remittent type. In children of low vitality and in old persons the disease may run its course virtually without fever. The pulse is increased in frequency, but unless the heart is seriously embarrassed, it is accelerated proportionately less than the respiration. In children the respiratory rate often reaches 70 or 80 per minute, the ratio between it and the pulse rate sometimes being 1 to 2 or even less than 2.

However, with failure of the right ventricle, the rate of the pulse may be 150 or even 170 per minute. Dyspnea is frequently marked. In children the alæ of the nose move actively and the accessory muscles of respiration are brought into play. Retraction of the base of the chest is not rarely observed. Cough of a painful character is usually present, although in infants and old persons this symptom may be entirely absent. The sputum is mucopurulent and sometimes blood-streaked or even rusty. In infants the expectoration is swallowed. If the patient is unable to expel the secretion from the bronchi or if a large area of the lung collapses the dyspnea and cyanosis may become intense. Pleuritic pain is much less common than in lobar pneumonia.

The digestive functions are often much disturbed and in some cases persistent vomiting or diarrhea is a troublesome feature. Nervous symptoms may be marked. In children, especially, there are likely to be restlessness, peevishness, insomnia and delirium. Occasionally the nervous phenomena are so obtrusive that meningitis is suspected. Examination of the blood usually reveals moderate polymorphonuclear leucocytosis. The urine shows the changes characteristic of febrile diseases.

In unfavorable cases the cough subsides, the respirations become more and more shallow, the cyanosis deepens, the pulse grows weaker, stupor supervenes, and death ensues from asphyxia.

*Physical Signs.*—If the pneumonic foci are small and discrete, which is frequently the case, the signs are simply those of a bronchitis extending into

the smaller tubes. In children, especially, the most careful examination often reveals nothing more than a few patches of fine subcrepitant râles in addition to the coarser râles of ordinary bronchial catarrh.

If a number of adjacent lobules are involved careful percussion may elicit areas of dulness in different parts of the lungs, especially near the bases. Even in the absence of dulness auscultation may reveal over the affected portions of the lung breathing that is harsh and more or less bronchial in character. Patches of collapse, if sufficiently extensive, also yield dulness on percussion, but the breath sounds over them are feeble or suppressed. In the pseudo-lobar form of the disease, in which the greater part of a lobe is consolidated, the physical signs are almost identical with those of croupous pneumonia, both conditions yielding dulness on percussion, bronchial breathing, and bronchophony over large areas of the lung.

**Duration.**—Favorable cases usually terminate in from ten days to three weeks. Not rarely, however, the disease pursues a subacute course, and six or eight weeks elapse before all local and constitutional symptoms disappear. Of the fatal cases, the majority terminate within two weeks, but some last only forty-eight hours, and others linger for several weeks. Relapse and recurrence are not uncommon.

**Complications and Sequels.**—Collapse of the lung, more or less extensive, is almost constantly present. Empyema is generally believed to be less common in the ordinary forms of bronchopneumonia than in lobar pneumonia, but Hardy[1] encountered it in 16 of 150 cases and Wollstein[2] in 12 of 100 cases. In the streptococcus interstitial bronchopneumonia that prevailed extensively in a number of the military camps during the winter of 1917–1918 empyema was an extremely frequent and fatal complication. Pericarditis, meningitis, and arthritis are occasionally observed. Pneumothorax has been noted in a few instances. Suppurating otitis media occurs somewhat frequently in young children. The termination of bronchopneumonia in abscess or gangrene sometimes occurs, but it is rare except in the aspiration and metastatic forms. The termination in chronic interstitial pneumonia is also rare. Formerly tuberculosis was regarded as not an uncommon sequel, but it is now believed to be an exceptional event. The large majority of cases going on to caseation and cavity formation are undoubtedly examples either of primary tuberculous pneumonia or of chronic, perhaps quiescent, tuberculosis upon which an ordinary bronchopneumonia has been engrafted.

**Diagnosis.**—In *simple bronchitis* the patient looks much less ill than in bronchopneumonia; the temperature rarely exceeds 102° F. and is often less than 101° F.; dyspnea is slight; cyanosis is absent; and the physical signs, with the exception of coarse râles, are negative. Generally, not much difficulty is experienced in distinguishing between bronchopneumonia and *lobar pneumonia*. In the latter, as a rule, the onset is abrupt, with a distinct chill; the temperature is high, remarkably even, and usually falls by crisis between the seventh and ninth days; and the physical signs indicate a single large area of consolidation. In cases of primary bronchopneumonia of the pseudo-lobar type and in atypical cases of lobar pneumonia mistakes are often unavoidable. *Acute tuberculosis bronchopneumonia* may be indistinguishable from simple bronchopneumonia until signs of softening and excavation have appeared. The detection of tubercle bacilli in the sputa is, of course, an absolute criterion, but this evidence is rarely available before the occurrence of softening. Involvement of the apices, profuse sweating, and rapid emaciation point to tuberculosis.

[1] Lancet, Sept. 24, 1904.
[2] Jour. of Exp. Med., vol. vi, 1905.

**Prognosis.**—Bronchopneumonia is a serious disease, especially in young children and in old persons. The mortality is influenced by many conditions, but the average is probably not less than 30 per cent. Primary cases occurring in children over 2 years of age who have been previously healthy are the most favorable. Bronchopneumonia complicating measles, whooping cough or diphtheria is extremely fatal. In cachectic subjects the prognosis is always grave. In individual cases occurring in children a pulse-rate above 150, a respiration rate above 60, signs of carbon dioxid poisoning, and severe gastro-intestinal disturbances render the prognosis very unfavorable. In aspiration pneumonia the outlook is usually bad.

**Prophylaxis.**—Persons at the two extremes of life and all others of low vitality who suffer from acute catarrhal conditions of the upper respiratory tract require especially careful attention owing to their pronounced tendency to develop bronchopneumonia. Infants should be kept away from patients with acute respiratory infections, and all persons, irrespective of their age, who develop bronchopneumonia in the course of such infections as measles, whooping-cough, and influenza should invariably be separated from other patients with these diseases.

**Treatment.**—The open cold-air treatment, referred to under "Lobar Pneumonia," is less generally applicable to cases of bronchopneumonia, although in some instances, especially of the primary form and of that running a protracted course, it is very effective. In all cases the sick room should be well supplied with fresh air without drafts. In the case of very young infants a moist atmosphere is sometimes of great benefit and this may be secured by generating steam in an ordinary croup kettle. But whether the air is made moist or not it should be kept pure and, if possible, at a temperature not exceeding 70° F. Heavy, cumbersome bed-wraps should be avoided.

The diet should consist of liquid or semiliquid food. For children of more than three years and adults milk, junket, broths, soft-boiled eggs, and gruels are usually suitable forms of nourishment. For bottle-fed infants the milk strength should be reduced, as a rule, about one-third. Water must be freely given. In the more severe cases alcohol, in the form of whisky or brandy, well diluted, often seems to be of service. From 15 to 20 minims (1.0–1.3 mils), every three hours, for a child of 3 years, is usually sufficient.

In the absence of any special indication for local treatment, it will only be necessary to provide ample protection for the chest, and this may be done satisfactorily by means of a light jacket of cotton-wool. When the bronchitic feature is pronounced and there is much cough, mild counter-irritation over the thorax is very useful. The desired effect may be produced by the application of mustard-plasters, care being taken to prevent them causing more than slight redness of the skin. Oil of turpentine, diluted with two parts of olive oil, and rubbed into the skin, is also a satisfactory means of producing rubefaction. Poultices of linseed meal or of clay through their weight make the breathing more difficult and are therefore harmful.

Hydrotherapy does good in many cases, especially in young children. As a rule, the tepid, warm or hot tub-bath, at intervals of from 3 to 6 hours, is the best form. Cold bathing, or even cold sponging, is not usually well-borne. If the patient's temperature is high and his extremities are cold, which is often the case at the onset of severe attacks, or if at any time his circulation becomes especially feeble, he may be plunged for a minute or two into a hot bath (105° F.—40.5° C.). In other cases brief tepid baths (80°–90° F.—26.5°–32.0° C.) or warm baths (95°–100° F.—35.0°–38.0° C.) frequently serve to lower temperature, allay restlessness and promote sleep.

Drugs, judiciously selected with reference to the peculiar features of each case, are of great value. If the bronchitic element is prominent and the chest is full of râles, expectorants may be given with advantage. The most generally useful expectorants are potassium citrate and ammonium chlorid. From 3 to 5 grains (0.2–0.3 gm.) of the former or from 1 to 2 grains (0.065–0.13 gm.) of the latter may be given every 2 or 3 hours to a child of three years. If the bronchial secretion is very abundant, tincture of belladonna 1 minim (0.06 mil) every two hours, is sometimes efficacious. If the child is unable to expel the accumulated mucus and the breathing in consequence becomes much embarrassed, an emetic dose of ipecac may afford relief. In debilitated children, however, the emetic should not be used. If the cough is very severe and persistent from 10 to 15 minims (0.06–1.0 mil) of paregoric may be given every two or three hours for a short period. Digitalis is indispensable when there are indications of circulatory failure. Two to three minims (0.1–0.2 mil) of the tincture every four hours is an average dose for a child of two years. For acute heart failure reliance must be placed upon subcutaneous injections of digipuratum or digalen, 1 to 2 minims (0.06–0.12 mil), camphor, ¼ to ½ gr. (0.015–0.03 gm.) in sterile olive oil, or epinephrin, 3 to 5 minims (0.18–0.3 mil). Tympanites is to be treated by the applications of weak sinapisms to the abdomen, by anemas of asafetida, by enteroclysis with warm saline solution, by the use of a rectal tube, or by subcutaneous injections of phystostigmin—$\frac{1}{500}$ grain (0.00013 gm.)—or of liquor hypophysis—1 to 3 minims (0.06–0.18 mil)—for a child of three years. Inhalations of oxygen sometimes lessen cyanosis and make the breathing easier. Strychnin, $\frac{1}{200}$ grain (0.0003 gm.) every three or four hours for a child of two years, is also of benefit in combating respiratory failure.

During convalescence tonics and a change of air are often required.

## STREPTOCOCCUS PNEUMONIA

During the winter of 1917–1918 there appeared in the United States and also to a less extent in France an epidemic type of pneumonia which was induced by *Streptococcus hæmolyticus*. The disease was especially prevalent in the military cantonments. Prior to 1917 outbreaks of this form of pneumonia seem to have been uncommon, although in 1916 Mathers[1] studied a series of cases in which the inciting microbe was a hemolytic streptococcus.

**Etiology.**—Streptococcus pneumonia usually occurs as a secondary process complicating or following one of the acute infectious diseases, especially measles, influenza or scarlet fever. In some instances it is superimposed upon ordinary pneumococcus pneumonia and occasionally it arises as a primary condition. The infection is transmitted chiefly from patient to patient and by healthy carriers who have been in contact with patients.

**Morbid Anatomy.**—In the majority of cases the lesions are those which MacCallum has described under the name of acute interstitial bronchopneumonia (see p. 588) and consist chiefly in a great infiltration of the bronchial walls and framework of the lung with mononuclear wandering cells. Macroscopically, the characteristic feature is the presence of prominent, gray, firm peribronchial nodules, with surrounding edema and hemorrhage. Less frequently there is a patchy lobular pneumonia or a diffuse infiltration resembling that of lobar pneumonia. Indeed, combinations of lobar pneu-

[1] Trans. Chicago Path. Soc., April 1, 1916.

monia caused by the pneumococcus and of interstitial bronchial pneumonia caused by the streptococcus are sometimes observed. Other peculiarities of the process are the rapidity with which exudates undergo organization and the marked tendency to complications.

**Symptoms.**—In the secondary cases the onset is usually indicated by an increase in the fever and the occurrence of cough, mucopurulent expectoration, and slight respiratory embarrassment. Primary cases begin insidiously, as a rule, with "sore throat" and cough, but occasionally the onset is abrupt with overwhelming prostration and symptoms suggestive of a general septicemia. When the disease is fully developed the chief symptoms are irregular fever (102°–104° F.), intense dyspnea, dusky cyanosis of the face, persistent cough, expectoration of mucopurulent, blood-streaked sputum, and extreme restlessness and anxiety. Delirium is frequently absent, although it sometimes occurs in cases near death. The **physical signs** are usually those of ordinary bronchopneumonia. Not rarely, however, signs of consolidation are wanting and the only objective finding is the presence of numerous râles of various types throughout the chest. In most cases there is a moderate polymorphonuclear leukocytosis.

Empyema is an extremely frequent complication. Pericarditis, otitis media, peritonitis, and abscesses in distant parts of the body may also occur.

The **diagnosis** rests upon the occurrence of large numbers of the hemolytic streptococcus in the sputum or the isolation of this organism from the blood, although bacteremia is frequently absent until a few hours before death. The **prognosis** is serious, the mortality in many outbreaks exceeding 50 per cent.

**Treatment.**—Prophylaxis and treatment are the same as for ordinary bronchopneumonia.

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## FRIEDLÄNDER'S BACILLUS PNEUMONIA

The Bacillus mucosus capsulatus identified by Friedländer in 1882 is not infrequently associated with ordinary pneumonia as a secondary invader. Occasionally it seems to be the sole etiological factor in pneumonia. In 1915 Sisson and Thompson[1] collected from the literature 33 authenticated cases of this kind. The disease occurs chiefly in late adult life and seems to be rare in children.

**Morbid Anatomy.**—The process at first usually shows a lobular distribution, but later it tends to become definitely lobar. The consolidated portion of the lung presents a mottled appearance and is of a peculiar grayish color. On cross-section the cut surface is moist, smooth or only slightly granular, and on compression of the lung yields a tenacious, slimy, sanguineous mucoid exudate. Abscess formation and necrosis are more common than in pneumococcus pneumonia.

Microscopically, the alveoli are found to contain numerous encapsulated bacilli, a loose net-work of fibrin, a variable number of red blood cells and polymorphonuclear leucocytes, and desquamated epithelial cells, some of which have fused to form phagocytic giant-cells.

**Symptoms.**—The symptoms and physical signs are similar to those of pneumococcus pneumonia, but the sputum is profuse, bloody, very slimy and non-purulent and contains enormous numbers of the infecting bacilli.

[1] Amer. Jour. Med. Sci., Nov., 1915.

Herpes labialis is rare, the signs of toxemia are marked and appear early, the course is comparatively short, and the outcome is almost invariably fatal. The diagnosis can be made definitely only by finding the Bacillus mucosus capsulatus in the sputum in great numbers or by identifying it in the blood. The presence of merely a few bacilli in the sputum is of little diagnostic significance.

**Treatment.**—The treatment is that of ordinary lobar pneumonia.

## ABSCESS OF THE LUNG

Abscess of the lung is comparatively rare. (1) It is an occasional seque of ordinary pneumonia, both lobar and lobular. (2) Not rarely it is a result of aspiration pneumonia, due to the inhalation of infective material from the upper respiratory tract—an accident more likely to occur if the reflex excitability of the parts is impaired, as in ether narcosis, the toxemia of the acute infectious diseases, and drunkenness. (3) The impaction of a foreign body, such as a seed, button, tack, etc., in one of the larger bronchi is responsible for a fairly large proportion of cases. (5) Pulmonary abscess sometimes arises from the extension of a suppurative process in a structure contiguous to the lung, as an empyema, abscess of the liver, subphrenic abscess, etc. (6) It may follow the lodgement of an infective embolus in the lung, as in ulcerative endocarditis or pyemia. (7) It may be a sequel of traumatic injury to the chest, such as a severe contusion or a penetrating wound. Of all these causes, the aspiration of infective material during an operation on the upper respiratory tract under a general anesthetic, especially tonsillectomy, probably ranks first in importance. In a series of 32 cases at the Massachusetts General Hospital, cited by Whittemore,[1] 21 (65 per cent.) were due this cause. The symptoms usually appear in from 4 to 10 days after operation. The least common cause of primary pulmonary abscess is ordinary pneumonia.

The infection is usually of the mixed type, with the streptococcus or staphylococcus predominating.

**Morbid Anatomy.**—Pulmonary abscess may be single or multiple. In 83 per cent. of 54 cases analyzed by Quincke,[2] and in 70 per cent. of 30 cases analyzed by Norris and Landis[3] a lower lobe was the site of the disease. However, postoperative aspiration abscess not rarely occurs in the upper lobe. The right lung is affected more frequently than the left and in the majority of cases the abscess is situated at the periphery of the lung. The solitary abscess usually varies in size from that of a cherry to that of an orange. Occasionally it involves a whole lobe. The cavity contains, as a rule, remnants of lung tissue as well as pus, and not rarely the contents are putrid. Acute abcesses are surrounded by an area of hemorrhagic pneumonic solidification, outside of which the lung for a variable distance is congested and edematous; chronic abscesses are usually delimited by a wall of fibrous tissue. Over a peripheral abscess the pleural surfaces are frequently adherent. Embolic abscesses are usually small, multiple and superficially located.

An abscess in the lung may rupture into a bronchus, and thus discharge its contents, leaving behind a suppurating cavity which in some instances is eventually obliterated through the contraction of enveloping scar tissue.

[1] Surg. Clin. of North America, June, 1921.
[2] Mitteil. aus den Grenzgebieten der Med. u. Chir., 1896, Bd. I.
[3] Trans. Assoc. Amer. Phys., 1913.

It may perforate into the pleura, and thus give rise to empyema or pyopneumothorax. Rarely it empties into the pericardium or esophagus. Purulent pleurisy may also occur without rupture of the abscess.

**Symptoms.**—Abscess of the lung is often suggested by the presence of one of the etiologic factors in association with symptoms referable to the lungs, such as cough, expectoration, dyspnea, and the general symptoms of septic infection—intermittent or remittent fever, sweats, rigors, leukocytosis, etc. In many cases the sputum furnishes the chief clue to the condition. It is usually abundant, purulent or muco-purulent, and of a mawkish sweet or offensive odor, although, as a rule, it is not so foul as in gangrene of the lung or long-standing bronchiectasis. Severe paroxysms of coughing with profuse expectoration are especially prone to occur when the patient turns suddenly on his healthy side. Microscopically, the sputum frequently shows elastic fibers with an alveolar arrangement—a feature of great significance. Crystals of hematoidin may also be present.

The **physical signs** are variable. In some cases there is a circumscribed area of dulness with distant bronchial breathing and fine bubbling or crepitating râles, in others, there are more or less definite signs of a cavity. The roentgen-ray often renders valuable aid in diagnosis, the usual finding being a round area of diminished density with a fluid level, or a more or less irregular area, very dense in the center and fading toward the periphery. Clubbing of the fingers may be an early feature.

Small multiple abscesses in the lung usually cannot be recognized with certainty, but their presence may be suspected in cases of focal suppuration if the patient develops a cough with profuse sanio-purulent expectoration or in cases of pneumonia if the usual symptoms of the disease are succeeded by those of general septic infection and the physical findings consist of scattered areas of dulness, with fine bubbling râles.

**Diagnosis.**—Pulmonary tuberculosis, pulmonary gangrene, encapsulated empyema, and bronchiectasis are the conditions with which abscess of the lung is most likely to be confused. In *pulmonary tuberculosis* there is usually a history of long-standing illness, the most advanced lesions are, as a rule, at the apex, and the sputum, if examined repeatedly, rarely fails to show tubercle bacilli. It must not be forgotten, however, that the two conditions not rarely co-exist; thus in a series of 56 cases of pulmonary abscess reported by Hedblom,[1] of the Mayo Clinic, there was evidence of primary or associated tuberculosis in 17. It is often difficult to distinguish abscess from *gangrene* even at necropsy, but clinically, extremely fetid expectoration and frank hemoptysis are in favor of gangrene.

*Encapsulated empyema* may closely simulate pulmonary abscess, but the former much more frequently succeeds ordinary lobar pneumonia than the latter. Moreover, empyema usually yields on x-ray examination a more clearly defined shadow than abscess and unless it is in communication with the lung it is less likely to be accompanied by copious fetid expectoration. A pronounced mixture of organisms in the sputum is in favor of abscess. The differentiation of pulmonary abscess from *bronchiectasis* is considered on p. 577.

**Prognosis.**—The prognosis is grave, although small solitary abscesses offer a fair prospect of recovery. Spontaneous cure occurs probably in from 5 to 10 per cent. of the cases of short duration. Multiple abscesses, especially if embolic, are almost invariably fatal.

**Treatment.**—The treatment of localized suppuration is free drainage. Recovery, complete or partial, occurs in about 40 per cent. of the cases. Lord[2]

[1] Medical Record, 1919, xcvi, 441.
[2] Med. Clin. of North America, Mar., 1919.

reports complete cure in 16 per cent. of 62 cases, and Hedblom[1] cure or improvement in 66.6 per cent. of 30 acute cases and in 41.1 per cent. of 17 chronic cases. The operative mortality in 600 cases analyzed by Külbs[2] was 17.5 per cent., in Hedblom's cases, 33.3 per cent., and in 31 cases, reported by Whittemore,[3] 16 per cent.

## GANGRENE OF THE LUNG

Gangrene of the lung is due to the action of saprophytic and other bacteria on a part of the pulmonary tissue the vitality of which has been destroyed or greatly reduced by an interference with its blood supply. It occurs under conditions similar to those which give rise to pulmonary abscess, which indeed it not infrequently follows. It sometimes supervenes upon ordinary pneumonia; rarely, however, unless the general nutrition has been previously impaired by old age, abuse of alcohol, or other disease, especially diabetes. Aspiration pneumonia is an important cause. In these cases the fetid material may come from the pharynx, from the esophagus, as when a cancer perforates into a bronchus, or from a bronchiectatic or tuberculous cavity. The impaction of a foreign body in a bronchus was the immediate cause in 31 cases collected by Clarke and Marine.[4] In rare instances gangrene results from the pressure of an aneurysm or tumor, pulmonary embolism, rupture of an empyema into the lung, or a wound of the lung. The infection is probably always polymicrobic (Ophüls[5]). Cases apparently caused by spirochetes and fusiform bacilli aspirated from infected gums have been reported.

**Morbid Anatomy.**—Two forms are recognized, the *circumscribed* and the *diffuse*, according as the process is or is not sharply defined. In either case the sphacelated tissue is usually surrounded by a zone of hepatized lung. Diffuse gangrene may involve a whole lobe, or even the greater part of a lung. The gangrenous mass is pulpy, of a brownish, greenish, or blackish color, and horribly offensive. In many cases the sphacelus ultimately undergoes complete disintegration and is expectorated. In this event there remains a cavity, partially filled with putrid liquid, and sometimes traversed by blood vessels of considerable size. Pleurisy is rarely absent. In many cases the pleural surfaces are adherent and somewhat frequently there is a pleural effusion. Rupture of the gangrenous mass into the pleura may give rise to pyopneumothorax. Secondary bronchopneumonia and putrid bronchitis are also common complications. Cerebral abscess is not very uncommon.

**Symptoms.**—The symptoms and physical signs of pulmonary gangrene are very similar to those of abscess of the lung. The sputum alone is characteristic. It is usually abundant, watery, of a dark brown or greenish color, and intensely fetid. On standing, it separates into three layers—an upper, frothy layer, a middle serous stratum, and a thick, greenish-brown sediment containing cellular detritus, hematoidin crystals, fat droplets, pigment granules, shreds of pulmonary tissue and numerous microörganisms. Elastic fibers with an alveolar arrangement are usually present. The breath of

[1] Med. Clin. of North America, Mar., 1919.
[2] Mitteil. aus den Grenze biet. der Med. u Chir., 1912, xxv, No. 3.
[3] *Ibid.*
[4] Amer. Jour. Med. Sci., Mar., 1906.
[5] Jour. of Med. Research, June, 1902.

the patient, as well as the sputum, is often so offensive that he becomes a burden to himself and his associates. Hemoptysis frequently occurs, owing to involvement of the blood vessels in the destructive process. Occasionally, there is no communication between the putrefactive area and a bronchus, and in consequence foul-smelling sputum and fetor of breath are absent from the beginning to the end of the process.

From uncomplicated *putrid bronchitis*, pulmonary gangrene is to be distinguished by the presence of elastic fibers or shreds of lung tissue in the sputum, and the marked tendency to hemorrhage.

**Prognosis and Treatment.**—The prognosis is grave. The mortality without operation is probably not less than 90 per cent. Surgical treatment is indicated if the lesion is solitary and can be located and if it is not a complication of an incurable disease. Nutritious food and stimulants are required to support the system. Inhalations of creosote or phenol may be employed to lessen the fetor of the breath.

## CHRONIC INTERSTITIAL PNEUMONIA

(Cirrhosis of the Lung; Pulmonary Fibrosis)

Chronic interstitial pneumonia is a productive inflammatory disease of the lung characterized by an overgrowth of connective tissue and obliteration of the alveoli. The process may be either circumscribed or diffuse.

**Etiology.**—Circumscribed areas of fibrosis are frequently found around quiescent tuberculous nodules, gummas, tumors, and echinococcus cysts. In other cases they represent the scars of healed infarctions, abscesses, or wounds. Diffuse fibrosis of the lung has a varied etiology. Its chief causes are:

1. *Inhalation of Dust.*—Dust is inhaled by everyone, but ordinarily the amount retained in the lungs is so small that it produces no injurious effects. Much the greater portion is caught in the secretions of the respiratory tract or is taken up by leucocytes or loose epithelial cells (dust-cells) and is ultimately expectorated. When considerable quantities of dust are breathed in for a long time, however, the lungs become thoroughly infiltrated with it and, owing to the mechanical irritation produced by the foreign particles, hyperplasia of the connective tissue results. Fibrosis from this cause is known as *pneumokoniosis*. In such cases some of the particles pass directly between the epithelial cells of the alveoli into the lymph-spaces, and are then taken up by the connective-tissue cells. Many particles are conveyed by wandering leucocytes to the lymphatics and are finally deposited, in the fibrous tissue of the lungs and in the peribronchial lymph-nodes which in consequence may be deeply pigmented and much enlarged. Occasionally the dust-particles escape from the lymph-nodes into adjacent veins and eventually find lodgment in the spleen, liver, and other organs.

Coal-dust pigmentation of the lungs, or *anthracosis*, is seldom entirely absent in adults, but in coal miners and coal heavers it often attains such a degree that the lungs become almost uniformly black. Cirrhosis of the lungs may also result from the infiltration of the pulmonary tissue with iron-dust (*siderosis*) or stone-dust (*chalicosis*).

2. *Pneumonia.*—Rarely in lobar pneumonia and still more rarely in bronchopneumonia, when resolution is long delayed, the exudate is gradually replaced by vascularized fibrous tissue. In this process the invading fibroblasts spring from the alveolar walls or walls of the bronchioles and the new

vessels from the preëxisting capillaries. Eventually the original exudate disappears, the overgrown fibrous tissue shrinks, and the thickened alveolar walls come together and adhere. As a result of these changes the affected part of the lung is transformed into a resistant, flesh-like mass.

3. *Atelectasis of the Lung.*—Persistent collapse of the lung resulting from compression of the pulmonary tissue by a collection of air or liquid in the pleural sac or from obstruction of a bronchus by a tumor or aneurysm is frequently followed by fibroid changes in the area affected. In these cases the epithelium of the alveoli degenerates, the alveolar walls coalesce, the connective tissue of the septa proliferates, and finally all semblance of pulmonary structure is lost.

4. *Pleurisy.*—Occasionally chronic pleurisy leads to cirrhosis of the lung more directly than by causing compression of the underlying pulmonary tissue. Thus, extension of the inflammatory process to the lung may take place by way of the interlobular and peribronchial lymphatics. In well-marked cases of this type (pleurogenic interstitial pneumonia) fibrous trabeculæ extend from the thickened pleura throughout the lung, dividing it into variously sized islands of pulmonary tissue. As a rule the alveolar structure is more or less compressed by the pressure of the surrounding trabeculæ.

5. *Chronic Congestion of the Lungs.*—Persistent engorgement of the pulmonary veins, such as occurs in chronic valvular disease, particularly in mitral regurgitation or stenosis, sometimes leads to a form of pulmonary cirrhosis, known as brown induration of the lungs. In this condition the overgrowth of connective tissue is associated with dilatation of the capillaries and hematogenous pigmentation of the cells. Macroscopically, the lungs are larger and firmer than normal and brownish-red in color.

6. *Pulmonary Tuberculosis.*—An overgrowth of connective tissue is almost constantly found among the lesions of chronic pulmonary tuberculosis, and in the form of the disease known as fibroid phthisis it may be the most conspicuous feature. In some instances a condition which is primarily a fibrosis may later become tuberculous, but much more frequently when the two conditions co-exist the tuberculous element is the primary one. Indeed, fibrosis arising from various causes, such as the inhalation of coal-dust, seems to retard the progress of tuberculous infection once this process gains a foothold in the pulmonary tissue.

7. *Pulmonary Syphilis.*—Gummata of the lung is not infrequently accompanied by a more or less diffuse cirrhosis, and according to Virchow, pulmonary syphilis occasionally begins as a chronic interstitial pneumonia. In these cases the process usually develops first at the root of the lung and extends inward along the bronchi and blood-vessels.

**Morbid Anatomy.**—The affected areas are firm, airless, scar-like, and of a grayish or slaty color. Occasionally, in advanced cases of diffuse cirrhosis an entire lung is reduced to a tough leathery mass no larger than the fist. The bronchi which are still pervious are usually dilated. Tuberculous lesions are often present, particularly at the apex, and when this is the case the fibrosis is usually the secondary process. The pleura is, as a rule, thickened and adherent. The uninvolved portions of the diseased lung and the opposite lung are emphysematous. The heart is usually drawn toward the affected side and may show enlargement of the right ventricle. In severe unilateral cases the affected side of the chest is retracted and the spine bent.

**Symptoms.**—The symptoms are mainly those of the co-incident emphysema and chronic bronchitis. Thus, there is *dyspnea,* which is rarely pro-

nounced except on exertion; *paroxysmal cough*, which is especially troublesome during exacerbations of the bronchial catarrh; and *expectoration*, which is usually mucopurulent and often profuse. In many cases the cough and expectoration are those of bronchiectasis. In well-marked anthracosis the sputa are dark gray, sometimes intensely black, and in other forms of pneumokoniosis the sputa may also contain particles of the foreign matter (oxid of iron, silica, etc.) which has been inhaled. Hemoptysis is not uncommon. There is rarely fever, and the general health of the patient may be well preserved for many years.

**Physical Signs.**—If the areas of cirrhosis are small and widely disseminated, as in many cases of pneumokoniosis, the only physical signs for a long time may be a somewhat harsh respiratory murmur with prolonged expiration and a few scattered râles, dry or moist, according to the character of attending bronchitis. In the later stages, however, the signs of emphysema and bronchiectasis are frequently present. In the cases of pulmonary cirrhosis following pneumonia or chronic pleurisy there is often marked deformity of the chest. The affected side is retracted, the shoulder is depressed, and the spinal column is curved, with the convexity toward the healthy side. The respiratory movements over the affected side are diminished or absent, while those of the sound side are exaggerated. The heart is displaced, being drawn toward the diseased side, and when the left lung is retracted the cardiac pulsations may be diffused over a very large area. The vocal fremitus over the cirrhotic lung is frequently increased, but when the bronchi are obliterated or the pleura is greatly thickened it may be diminished or abolished. The percussion note is usually dull, especially at the base, but it may be tympanitic or amphoric over areas enclosing large bronchiectatic cavities. The respiratory murmur varies with the condition of the bronchi and pleura. It may be weak, bronchial or cavernous. The pulmonic second sound of the heart is often accentuated. Clubbing of the fingers is frequently observed in cases with bronchiectasis.

**Diagnosis.**—It may be impossible to exclude *fibroid phthisis*, except by the persistent absence of tubercle bacilli from the sputum, but restriction of the physical signs to the base of a lung, especially if the constitutional symptoms are comparatively mild, is always in favor of a non-tuberculous fibroid condition.

**Prognosis.**—The disease is incurable, although it may be well borne for many years. Death may result from dilatation of the right ventricle, intercurrent disease, or rarely hemoptysis. Tuberculosis does not usually develop as a secondary process. Indeed, so far as pneumkoniosis is concerned statistics seem to indicate that certain forms of dust infiltration may actually lessen the disposition to tuberculosis or retard its progress. According to the last U. S. census report, pulmonary tuberculosis caused 9.6 per cent. of all deaths among miners and quarrymen as against 14.5 per cent. for all occupied males, and as against 11.2 per cent. for all outdoor workers.

**Treatment.**—The treatment is chiefly that of chronic bronchitis and pulmonary emphysema.

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## PULMONARY EMPHYSEMA

As applied to the lungs the term emphysema (from ἐν and φυσάω—I blow into) is used to designate two distinct conditions: (a) An infiltration of air into the connective tissue of the lungs; (b) an abnormal distention of the

air-sacs of the lungs. The first of these affections is known as *interstitial* or *interlobular emphysema;* the second as *vesicular emphysema.*

**Interstitial or Interlobular Emphysema of the lungs** is comparatively rare and is usually due to rupture of the air-vesicles. Such an accident may result from a penetrating wound or contusion of the chest, from violent coughing, as in whooping-cough, or from severe straining efforts, as in difficult parturition. When there is extreme atrophy of the interlobular septa, as in vesicular emphysema, or necrosis of the pulmonary parenchyma, as in abscess of the lung, rupture may take place spontaneously. From the interior of the lung the air usually works its way to the connective tissue immediately beneath the pleura, where it appears in the form of small blebs, movable from place to place. If the rupture occurs near the root of the lung the air may extend to the mediastinum and thence to the subcutaneous tissue of the neck and chest.

Interstitial emphysema produces no characteristic symptoms, and clinically is of little interest. Unless the subcutaneous tissue is also involved, it can scarcely be recognized during life.

**Vesicular Emphysema** may result from increased pressure within the alveoli or from degenerative changes in the walls of the alveoli, with loss of elasticity, or from both of these factors acting conjointly. Acute over-distention of the air-vesicles is frequently met with in children in consequence of whooping-cough or bronchopneumonia. In these affections the powerful inspiratory and expiratory efforts attending the coughing spells force the air into those portions of the lung in which there is least resistance, and thus dilate the vesicles beyond their normal capacity. This excessive distention of the lungs, which is sometimes called **acute vesicular emphysema,** is not particularly serious, for the air-vesicles not being altered in structure usually return to their normal size with the cessation of the cough. A somewhat similar condition, known as **compensatory emphysema,** develops in certain portions of the lung when, from any cause, other portions become atelectatic or solidified. In this case extra work is thrown upon the parts that remain active, and if the strain is not too severe, a true hypertrophy may ensue. Thus, when one lung is completely incapacitated by pneumothorax, pleuritic adhesions or pressure upon a main bronchus by an aneursym or tumor, it is not uncommon to find the other performing the function of both. Over the active lung the respiratory movements are increased, the percussion note is hyperresonant, and the vesicular murmur is exaggerated. Eventually, if the cause continues to operate, the parenchyma of the distended lung may undergo atrophy and lose its elasticity, in which case actual substantive emphysema is produced.

In old age the pulmonary tissue, in common with other tissues, undergoes atrophy, and in consequence the air vesicles increase in size, even though they are not subjected to any unusual distending force. Owing to the progressive wasting of the intervesicular septa, however, the volume of the lungs is not increased; on the contrary, it is diminished. To this condition, which is essentially the product of involution, the term **atrophic** or **senile emphysema** (**small-lunged emphysema of Jenner**) has been applied. When well developed, it is readily recognized. The chest is small and narrow, the thoracic walls are thin, and the ribs are oblique. Percussion yields exaggerated resonance and auscultation feeble breathing with prolonged expiration. Dyspnea is rarely noticeable unless the patient exerts himself.

Lastly, there is a form of emphysema which is characterized by permanent overdistention of the air-sacs and marked increase in the volume of the lungs.

This form of the disease is spoken of as **hypertrophic, substantive,** or **large-lunged emphysema.** It is by far the most important, and the one usually implied when the term "emphysema" alone is used.

## Hypertrophic Emphysema

**Etiology.**—Hypertrophic emphysema is usually a disease of middle and advanced life. It is rare in childhood. It is more frequent in men than in women. Among predisposing causes, diseases that lead to repeated paroxysms of cough or persistent dyspnea, such as chronic bronchitis and asthma, rank first in importance. Occupations requiring prolonged and heavy muscular exertion also favor the occurrence of emphysema. Such callings as glass-blowing and wind instrument playing are usually cited as being especially liable to provoke the disease, but Prettin found only 5 cases of emphysema among 230 glass-blowers and Fisher did not find a single case among 500 members of military bands.[1] As conditions which increase the intravesicular tension bring on emphysema much more quickly in some individuals than in others, it has been surmised that a developmental defect in the lung, possibly a congenital hypoplasia of the elastic tissue (Cohnheim, Orth), is an important factor in the production of the disease. This view receives some support from the fact that in certain families several members have been observed to suffer in succession. Freund ascribed the disease to premature ossification of the costal cartilages, but this view has few adherents.

**Pathogenesis.**—The question whether permanent dilatation of the vesicles and loss of elasticity in the lung result immediately from forced inspiratory efforts, rendered necessary by dyspnea from any cause; from forced expiratory efforts as in coughing, asthmatic breathing, lifting heavy weights, etc.; or from weakness of the pulmonary tissue itself, as consequence of degenerative changes or developmental defects, cannot be definitely answered. It is likely that in many cases all three factors are operative. If one is first in importance it is probably forced expiration with the glottis closed or partially closed, as in coughing. In this effort the air, which cannot escape outward, is driven into the upper parts of the lung, where it stretches the alveolar walls beyond their normal limits, and finally destroys their elasticity. Unquestionably, when once emphysema is set up, the extension of the process is favored by the obliteration of the capillaries, which is consequent upon the increased pressure and distention of the alveoli.

**Morbid Anatomy.**—The disease usually involves the greater part of both lungs, though it may be circumscribed. Even when it is more or less general, the apices and anterior borders are more affected than the parts which receive support from the sides of the chest and diaphragm. When the thorax is opened the lungs are found to be enlarged, the pericardial sac in many cases being completely hidden. On removal they collapse imperfectly, or not at all. When the process is well advanced large bullæ or blebs, varying in size from a pea to a walnut, may be seen along the free borders. These bladder-like appendices are formed by the fusion of a number of alveoli and infundibula. The emphysematous tissue is pale, dry, and bloodless. It pits on pressure and when handled feels like a cushion of down (Laennec).

Microscopic examination reveals enlargement of the alveoli and infundibula and atrophy of the interalveolar septa. In many places the septa are perforated or partially destroyed, so that a single cavity often occupies the

[1] Münch. med. Woch., 1904, No. 6.

space of several alveoli. In advanced cases the partitions between the infundibula also disappear, and thus are produced the large sacs which are visible to the naked eye. The capillaries in the alveolar walls are attenuated and less tortuous than in the normal state. In many places they are transformed into impervious cords or are wholly obliterated. The epithelial cells of the alveoli are fatty and in part detached. Eppinger laid much stress upon the early disappearance of the elastic fibers, but according to a number of authorities (Klaesi, Ribbert, Sudsuki, Spalteholz) who have reinvestigated the subject, these fibers only share in the atrophic process to the same extent as the other tissues.

**Associated Lesions.**—Dilatation of the smaller bronchi is a frequent concomitant of alveolar ectasis. Obliteration of the vesicular capillaries leads to collateral hyperemia of the larger bronchi and thus bronchitis may be a consequence of emphysema, as well as an exciting cause of the disease. Obstruction to the pulmonary circulation, if marked, also brings about important changes in the heart, the chief effects being hypertrophy and dilatation of the right ventricle and auricle and enlargement of the tricuspid orifice. The other organs commonly present evidences of venous stasis.

**Symptoms.**—Dyspnea is the chief subjective symptom. It depends partly upon the inelasticity of the lung and partly upon the destruction of the alveolar capillaries. At first it is not marked, but as the disease advances it becomes more and more urgent, especially on exertion. Distinct asthmatic seizures are also of frequent occurrence. These may be attacks of true bronchial asthma, with which emphysema is often concomitant, but in some cases they are merely exacerbations of simple dyspnea resulting from intercurrent attacks of acute bronchitis, and in other cases they are paroxysms of so-called cardiac asthma. Cough is rarely absent, but it is rather the result of an accompanying bronchitis than of the emphysema itself. Owing to an aggravation of the catarrh, both the cough and dyspnea are especially severe in winter. In warm, dry weather many patients are comparatively comfortable. Expectoration may be scanty or copious according to the nature of the catarrh. Cyanosis is sometimes very pronounced, especially during the asthma-like paroxysms. It depends upon insufficient oxidation of the blood in the lungs. Late in the disease symptoms of general venous congestion and edema of the limbs may supervene in consequence of dilatation of the right ventricle.

**Physical Signs.**—In advanced cases the deformity is so characteristic that the disease is often revealed upon the first glance. The shoulders are high and stooped, the neck is short, the sternocleidomastoid muscles are prominent, and the veins of the neck are distended. The chest is said to be "barrel-shaped." It is somewhat short, but much increased in circumference. The antero-posterior diameter is especially long, being almost equal to the transverse diameter; hence the cyrtometric tracing approaches a circle. The sternum is pushed forward and the spine is strongly arched. The ribs are more horizontal, the interspaces are wider, and the epigastric angle is more obtuse than in the normal chest. This peculiar configuration of the chest is to be attributed more to the powerful contractions of the inspiratory muscles than to the pressure of the lungs from within.

Inspiration is short and labored, expiration is prolonged. Notwithstanding the vigorous respiratory movements, the chest does not expand, but being unusually rigid rises and falls as a whole. The apex beat of the heart is rarely perceptible, but a distinct pulsation is frequently present in the epigastrium.

Palpation confirms the evidences afforded by inspection, and also reveals a diminution or absence of vocal fremitus. Percussion shows an extension of the lung boundaries in all directions. The area of cardiac dulness is diminished or abolished, and, owing to the low position of the diaphragm, the areas of hepatic and splenic dulness are depressed. The percussion note is hyperresonant, and may even be tympanitic.

The most characteristic auscultatory sign is weakness of the breath sounds with marked prolongation of the expiratory phase. At times the breath sounds may be completely concealed by whistling or cooing râles, the result of concomitant bronchitis or asthma. The heart sounds are usually obscured by the distended lung, although the pulmonary second sound is sometimes accentuated, owing to the increase of pressure in the pulmonary artery.

**Complications.**—Excepting *bronchitis*, *asthma* and *dilatation of the right ventricle*, which have already been mentioned, there are few complications. Occasionally an emphysematous bleb gives way and in consequence *pneumothorax* or *interstitial emphysema* supervenes, according as the air ascapes into the pleural cavity or into the connective tissue of the lung. A few instances of severe and even fatal *hemoptysis* in emphysematous subjects are on record, but in none is it convincingly shown that the hemorrhage was the result of the emphysema itself.

**Prognosis.**—Hypertrophic emphysema is incurable, yet in many cases it is does not materially shorten life. When it is possible to protect the patient from the vicissitudes of weather, he may be kept fairly comfortable for many years. Death usually results from intercurrent disease, but it may be due to dilatation of the heart and failing compensation.

**Treatment.**—The treatment of emphysema is chiefly that of the accompanying disease. The various means suggested for relief of chronic bronchitis may nearly always be used with advantage. If asthma is the primary disease, treatment directed toward lessening the frequency and severity of the paroxysms should be instituted. Violent exercises and over exertion of all kinds must be proscribed. A diet that is light and sustaining is indicated. All foods likely to induce flatulence should be avoided. Much benefit is often derived from a change of climate, the choice of locality, however, depending somewhat upon the character of the complicating bronchitis. As a rule, high elevations are to be avoided.

The inspiration of compressed air with expiration into rarefied air by means of the pneumatic cabinet has been employed with variable degrees of success. Strümpell speaks favorably of rhythmic compression of the lower portion of the thorax during expiration, as recommended by Gerhardt. This should be done systematically by another person two or three times a day during fifty or sixty respirations.

Tonics, such as iron and cod-liver oil, are required in some cases to improve the general health. Strychnin, being both a general tonic and a respiratory stimulant, is particularly useful. Digitalis is often of service when signs of cardiac insufficiency appear. Ammonium carbonate, in conjunction with strychnin and digitalis, usually has an excellent effect upon acute exacerbations of the bronchial catarrh. At such time sinapisms applied to the chest may also afford considerable relief. If sleep is disturbed by troublesome cough and oppressive dyspnea it may be necessary to give codein, heroin or even morphin. When the breathing is very difficult, the face suffused and livid, and the pulmonary circulation much impeded, recourse should be had to blood-letting, either local or general, according to the urgency of the symptoms.

## EDEMA OF THE LUNGS

The term edema of the lungs is applied to the presence of serous fluid in the air-vesicles, or in the air-vesicles, finer bronchial tubes and interstitial tissue of the lungs. It may occur as a part of a general dropsy, or as a purely local condition. It may be diffuse or circumscribed, acute or chronic.

**Etiology.**—Pulmonary edema is especially common in cardiac disease with failing compensation, acute and chronic nephritis, and cachectic states. As a terminal or agonal condition it occurs in a great variety of diseases, both acute and chronic. A circumscribed form is frequently observed around areas of pneumonia, pulmonary abscesses, etc. An acute edema of the lungs is sometimes caused by mechanical obstruction of the pulmonary vessels by a thrombus or embolus. Not rarely it develops very suddenly, even without warning, and with slight provocation, in the course of cardiovascular disease or chronic nephritis with arterial hypertension. This type of acute edema, because of its marked tendency to recur, has been designated *paroxysmal pulmonary edema*. It is usually nocturnal. In a case reported by Lissaman[1] there were 72 attacks in 2½ years and in one attack the patient expectorated more than 1200 c.c. of fluid in a few hours. Acute pulmonary edema sometimes develops in the course of acute infectious diseases, such as pneumonia, influenza, small-pox, etc. It was very common in the influenza prevailing in 1918–1919. It may occur as a result of the inhalation of irritant gases or vapors; it is sometimes seen in cases of head injuries or acute cerebral disease; and occasionally it is met with as an expression of angio-neurotic edema. Finally, acute edema of the lungs with profuse albuminous expectoration rarely occurs immediately after the aspiration of a pleural effusion or after even the tapping of the abdomen for ascites (Pinaut, Joucla).

**Pathogenesis and Morbid Anatomy.**—The pathogenesis of diffuse pulmonary edema is somewhat obscure. Welch's theory, however, has obtained wide acceptance. According to this theory the essential factor in a large group of cases is a "disproportion between the working power of the left ventricle and of the right ventricle of such a character that, the resistance remaining the same, the left heart is unable to expel in a unit of time the same quantity of blood as the right heart." As a result of the relative weakness of the left ventricle engorgement of the pulmonary vessels ensues with transudation of serum through the capillary walls into the alveoli and alveolar walls. According to some authors, toxic agents acting in some obscure manner, possibly by increasing the permeability of the pulmonary vessels, may be a subsidiary cause. In some cases the edema is undoubtedly of inflammatory origin. In this class are most of the cases occurring in the acute infections. Possibly in rare instances infections edema of the lungs may arise as a primary condition.

The edematous lung is usually pale, although it may be abnormally red from congestion. It is distended and heavy, crepitates less than normal lung tissue, pits on pressure, and when cut discharges a large quantity of frothy, often blood stained, serum. As a rule the bases are the parts most affected.

**Symptoms.**—Increasing dyspnea and cough are the most conspicuous symptoms. The cough may be dry, but usually it is accompanied by more or less abundant foamy, serous expectoration, sometimes tinged or streaked with blood. Fever is absent except in cases that are frankly inflammatory. Numerous moist râles, both fine and coarse, are constantly present, and when the condition is well developed there may be slight dulness and weakening of the respiratory sounds over the postero-inferior portions of the lungs.

[1] Lancet, Feb. 8, 1902.

In *acute paroxysmal edema* the patient is suddenly seized with cough, a sense of suffocation, and oppression of breathing, which soon becomes extreme. The expression is anxious, the face is pale or livid and the skin is cold and bedewed with sweat. The cough is at first dry, but later it is accompanied by profuse, frothy, blood-tinged expectoration. The pulse is frequent, and usually weak, although it may be full and strong. Over the chest there are numerous small bubbling and sibilant râles. The attack may result in death within half an hour, or the symptoms may continue for several hours and then gradually subside. In many cases there are repeated attacks at intervals of days, weeks or months during a long period of time. Between the attacks the patient may feel perfectly well, but more frequently he gives evidences of some cardiac insufficiency. The condition appears to be closely related to, if not identical, with that described as cardiac asthma. In some cases it is associated with angina pectoris.

**Diagnosis.**—The diagnosis is not difficult. In *ordinary bronchial asthma* the dyspnea is mainly of the expiratory type, musical râles predominate, and expectoration does not usually begin until the paroxysm subsides and even then it is often limited to glairy mucus. In *pulmonary infarction* the expectoration consists chiefly of thick, dark, non-aërated blood, and the dyspnea is usually accompanied by severe pain in the side.

**Prognosis.**—The prognosis is grave, not only because the condition in itself is a dangerous one, but because the primary disease of which the edema is an expression is usually one in which there is little prospect of cure. However, recovery from the edema is by no means uncommon.

**Treatment.**—The treatment of chronic pulmonary edema coincides with that of the underlying disease. Cardiac stimulants are nearly always indicated. If the symptoms are severe aromatic spirit of ammonia may be given by the mouth and camphor subcutaneously. Dry or wet cupping of the chest is often very useful. Except in feeble subjects active purges may also be used.

The treatment of acute paroxymal edema must be prompt and energetic. A subcutaneous injection of atropin ($\frac{1}{100}$–$\frac{1}{80}$ grain—0.00065–0.0008 gm.) and morphin ($\frac{1}{6}$ gr.—0.01 gm.) is often very effective. It should be given at once and repeated in half an hour, if necessary. At the same time aromatic spirits of ammonia or brandy should be given by the mouth. Nitroglycerin may be of service if the arterial tension is high. Oxygen may afford some relief. Counter-irritation by dry or wet cups or sinapisms is very useful, but when there is marked cyanosis venesection is preferable. The after treatment consists of rest, careful regulation of the diet, and, if there are symptoms of cardiac insufficiency, the use of such drugs as digitalis, caffein, strychnin, etc.

## HEMOPTYSIS

**Etiology.**—Hemoptysis, or blood-spitting, is most frequently caused by: (1) *pulmonary tuberculosis*. It occurs sooner or later in from 40 to 60 per cent. of all cases of this disease. Not rarely it is the first symptom to attract attention, and it may occur long before any physical changes in the lungs can be demonstrated. Hemorrhage was the initial symptom in more than 9 per cent. of 2000 cases of tuberculosis analyzed by Reiche.[1] Hemoptysis occurring in the absence of any obvious cause should be regarded as a symp-

[1] Zeit. f. Tuberk. u. Heilst., Bd. iii.

tom of tuberculosis until it can be proved to be of other origin. The bleeding occurring early in the disease it is usually slight and caused by the erosion of capillaries. The hemorrhages in advanced cases, however, are often profuse, being usually due to the rupture of exposed arteries in the walls of cavities.

Pulmonary hemorrhage is often excited by (2) *passive congestion of the lungs*, the result of chronic cardiac disease, especially lesions at the mitral orifice. According to Fagge and Sansom at least 18 per cent. of all cases of mitral stenosis are attended with the occasional expectoration of blood.

Less frequently hemoptysis results from (3) *certain other affections of the lungs*, such as infarct, tumor, abscess, gangrene, actinomycosis or hydatid cyst. Large quantities of pure blood are sometimes expectorated in pneumonia, but as a rule, the sputum in this disease is merely tinged with blood. Hemoptysis is a conspicuous symptom also in pulmonary distomatosis, a disease endemic in China and Japan, and excited by a trematode, Paragonimus westermanii. It frequently follows (4) *mechanical injuries of the chest*, such as blows and wounds.

Hemoptysis is sometimes caused by *ulcerative processes* in *the larynx, trachea* or *bronchi*. It is by no means uncommon in bronchiectasis. It is occasionally caused by (6) the rupture of *an aneurysm of the aorta, innominate artery or pulmonary artery* into the air-passages. In such cases the hemorrhage is usually sudden and fatal, but sometimes slight bleeding occurs for weeks or months before the final catastrophe. Bleeding from the lungs may occur in (7) *general diseases characterized by certain deficiencies in the blood*, such as scurvy, hemophilia, purpura hemorrhagica, and profound anemias.

Finally, hemoptysis in rare instances follows (8) the *arrest of the menstrual flow* and in such cases it is usually regarded as vicarious. However, both the amenorrhea and the hemoptysis are frequently the result of pulmonary tuberculosis.

**Symptoms.**—Sometimes the bleeding is preceded by irritative cough, dyspnea, or a feeling of oppression in the chest, but very often there is no premonition, the mouth being suddenly filled with warm salty fluid, which proves to be blood. The hemorrhage is rarely profuse unless it results from the rupture of an aneurysm or a large vessel in advanced tuberculosis. There may be only one hemorrhage, but more frequently there are recurrent attacks at intervals varying from a few hours to several days. The blood is usually raised by coughing, and is bright red in color, frothy, and alkaline in reaction. As a rule, it is mixed with more or less mucus. For some time after the hemorrhage auscultation of the chest reveals coarse and fine bubbling râles, due to the presence of blood and mucus in the bronchi. Complete physical examination should never be attempted until the bleeding has entirely ceased.

If hemoptysis is profuse some of the blood may be swallowed, and in this event hematemesis may occur, or the stools subsequently may appear black. For several days after the attack the sputa may be stained with altered blood or may contain small clots. The differentiation between hemoptysis and hematemesis is not usually difficult (see p. 450).

**Prognosis.**—Except in cases of aneurysm and of advanced pulmonary tuberculosis hemoptysis rarely proves immediately fatal. When death does occur it is the result of suffocation or of acute anemia. Frank hemorrhage in pulmonary tuberculosis may be followed by an improvement in the patient's condition, although not infrequently it seems to result in a rapid extension of the tuberculous infection. Bronchopneumonia may also occur

as a consequence of the aspiration of infected blood into healthy portions of the lung.

**Treatment.**—Absolute rest is imperative. An ice-bag may be placed over the suspected site of the hemorrhage, but it is of doubtful value and should be removed if it aggravates the cough. Morphin, in doses of 1/12 to 1/8 grain (0.005–0.008 gm.) hypodermically is of value in that it promotes tranquility and lessens irritative cough. Large doses, however, are objectionable, especially in tuberculosis, as they favor the retention of infected blood in the bronchi. Nitroglycerin is strongly recommended. It may do good by lowering the pressure in the pulmonary vessels. Small repeated hemorrhages seem to have been controlled in some instances by the use of saline purges. Among other remedies for which success has been claimed in long-continued bleeding, oil of erigeron, oil of turpentine and fluidextract of hamamelis may be mentioned. Ergot and tannin are useless and so is the inhalation of vaporized solutions of astringent drugs. Unless collapse is imminent stimulants of all kinds should be avoided. In cases of profuse hemorrhage bandages or elastic bands may be placed around the extremities, using sufficient pressure to impede the venous return without obstructing the arterial circulation. Artificial pneumothorax should be favorably considered in pulmonary tuberculosis if hemorrhages persist despite the usual methods of treatment and the site of the bleeding can be definitely determined.

## PULMONARY EMBOLISM, THROMBOSIS AND INFARCTION

Occlusion of the pulmonary artery or its branches may be caused by an embolus or by a thrombus. *Pulmonary emboli* are usually derived from coagula originating in one of the systemic veins, the right auricle, the right ventricle or the main trunk of the pulmonary artery. Emboli of this nature are common in chronic heart disease especially in lesions of the mitral valves. They not rarely occur after operations on the abdominal or pelvic organs and after child birth. They occasionally follow thrombosis of the veins of the leg in typhoid fever and other infections. Much less frequently pulmonary emboli are composed of fragments of tumors (carcinoma or sarcoma) that have penetrated a vessel wall. Fat embolism of the lung is an occasional complication of fractures. Garnier[1] in 1905 found 12 cases of hydatid embolism of the pulmonary artery on record.

Thrombosis of the pulmonary artery or its main branches is comparatively rare. It is observed chiefly in chronic heart disease and in general infections, especially typhoid fever. Occasionally it is the result of a pleuritic effusion or intrathoracic tumor.

Embolism or thrombosis of the larger pulmonary arteries usually results in *hemorrhagic infarction of the lung*. Occlusion of the main trunk of the pulmonary artery, however, may kill before an infarct has had time to form. Infarcts occur most frequently in the lower portions of the lung, and in the large majority of cases are at the periphery of the organ. In typical cases they are sharply defined, firm, and wedge-shaped, with the base of the wedge toward the surface of the lung. They are rarely larger than a hen's egg and usually are much smaller. The pleura over them is, as a rule, roughened by a deposit of fibrin. The color of the affected area is at first dark red, but it soon becomes reddish brown. Microscopic examination shows an extensive infiltra-

[1] Presse Médicalé, 1905, No. 47.

tion of the alveoli and septa with red-blood cells and more or less necrosis of the pulmonary tissue. After the infarct has existed for a time it may undergo absorption and be replaced by cicatricial tissue. If it is caused by an infected embolus, however, as in cases of pyemia or ulcerative endocarditis, it may result in abscess, pneumonia or pleurisy.

**Symptoms.**—Symptoms may be absent if the infarct is small and non-infective. Infarcts of moderate size usually give rise to pleuritic pain, dyspnea and cough. Occasionally, there is also a chill. Especially significant, however, is the expectoration of dark blood, pure or intimately mixed with mucus, a few hours after the sudden occurrence of pain in the side and dyspnea. The sanguineous expectoration often continues for several weeks. Fever is usually absent unless the embolus is infective. The physical signs are not very characteristic. Large peripheral infarcts may give rise to a circumscribed area of dulness, a friction rub, crackling râles, and feeble breath sounds. The presence of cardiac disease or of peripheral venous thrombosis, or the occurrence of the pulmonary symptoms soon after an abdominal operation makes the diagnosis of infarction of the lung, of course, more certain.

Obstruction of the main trunk or of a large branch of the pulmonary artery causes precordial pain and distress, intense dyspnea, lividity or pallor, anxiety, cold sweats, irregular heart-action, unconsciousness, with or without convulsions, and death within a few hours. Occasionally death ensues almost instantaneously. The etiologic factors may suggest the diagnosis, although the symptoms very closely resemble those produced by occlusion of the coronary arteries.

The **prognosis** of pulmonary infarction depends upon the size of the vessel occluded and the nature of the obstruction. Small aseptic infarcts are frequently absorbed.

**Treatment.**—Absolute rest is the most important safe-guard against the occurrence of embolic processes in all conditions in which thrombi are likely to form. After the actual occurrence of pulmonary infarction the treatment is entirely symptomatic. Stimulants may be required to combat cardiac failure and sedatives, especially morphin or codein, to relieve pain, cough and extreme restlessness.

## TUMORS OF THE LUNG AND PLEURA

Intrathoracic tumors are almost always malignant. Occasionally, however, **dermoid cysts** invade the lung from the mediastinum and in rare instances **papillomas** arise in the trachea or bronchi. Malignant disease may be primary or secondary. **Secondary carcinoma** is relatively common. It may arise from an initial focus in one of the abdominal organs, but more frequently it results from the extension of a primary mammary, esophageal, or thyroid tumor. The metastases may be grossly nodular or miliary. **Secondary sarcoma** most frequently originates in a primary growth in the marrow cavity of one of the long bones. Two autonomous formations approaching closely both carcinoma and sarcoma in their morphologic characteristics and appearing often as secondary tumors in the lungs are the **hypernephroma** and the **malignant deciduoma (choriocarcinoma)**. Of 22 cases of hypernephroma collected from the literature by Woolley[1] there were metastases in the lungs in 13. Malignant deciduoma involves the lungs secondarily in nearly 50 per cent. of the cases.

[1] Amer. Jour. Med. Sci., 1903, cxxv.

**Primary carcinoma of the lung** is comparatively rare, forming about 1.5 per cent. of all cancers. Sailer and Torrey[1] collected statistics showing 130 primary carcinomas of the lung in 87,451 necropsies, which compares with von Wiczkowski's[2] report of 125 cases in 58,497 necropsies. The tumor may have its source in the bronchial epithelium, bronchial mucous glands or avleolar epithelium. It may appear as a rounded mass near the hilus or as a diffuse lobar infiltration. Metastases are usually widespread, but they were absent in 33 of 374 cases analyzed by Adler.[3]

**Primary sarcoma of the lung** is very rare, many of the reported cases apparently having been atypical carcinomas, pulmonary extensions of pleural endotheliomas, or sarcomas secondary to growths in the mediastinal lymph-nodes, thymus, etc. True sarcoma of the lung may have its source in the pulmonary connective tissue or peribronchial lymph-nodes. It may be composed of spindle cells or round cells, and is usually limited to one lung. Metastases, except to the mediastinal lymph-nodes, are uncommon.

**Pleural endothelioma** has been somewhat frequently reported. It arises in the cells of the subpleural lymph spaces (Wagner, Volkmann, Adler), possibly on the basis of an inflammatory hyperplasia, and almost always over an extensive area. It begins as multiple nodules, which subsequently fuse and usually invade the lungs. Extension to the pericardium or peritoneum may occur and metastases may appear in the regional lymph-nodes, abdominal viscera or meninges.

Thoracic tumors occur more frequently in males than in females. The age of greatest incidence is between 20 and 60 years. Sarcomas occur at somewhat earlier ages than carcinomas. A number of cases of round-cell sarcoma have been reported in children.

**Symptoms.**—The dominant symptoms of intrathoracic malignant tumor may be those of a progressive consolidation of the lung, of stenosis of the larger bronchi or trachea, or of pleurisy with effusion. Cough and dyspnea are rarely absent. The cough varies in severity and quality according to the size and location of the growth. It is especially marked when the larger bronchi are involved or the mediastinum is invaded and the trachea compressed. In the latter event the cough is likely to be paroxysmal and of a ringing quality, as in aneurysm of the thoracic aorta. On the other hand, when the tumor is confined almost entirely to the vesicular structure the cough may be very slight. There is also much variation in the degree of dyspnea. When the tumor is at the hilus or is accompanied by a large pleural effusion it may be intense, and for a long period the only obtrusive symptom. Expectoration occurs in a large proportion of cases, but it may be slight or even absent. Stokes laid much stress upon the occurrence of a gelatinous reddish (currant-jelly) or brownish-black (prune-juice) sputum, but sputum of this character is only occasionally observed and, moreover, is not peculiar to pulmonary tumors. Exceptionally, disintegration of the tumor gives rise to copious fetid expectoration resembling that of gangrene. In a few instances the diagnosis has been made certain by the microscopic examination of tissue fragments in the sputum.

Hemoptysis, from congestion of the tissues surrounding the tumor or erosion of medium sized pulmonary vessels, is present in the majority of cases, and may be profuse and persistent. Pain is inconstant. It is often severe, however, when the pleura is involved or the thoracic nerves are compressed. Recurring attacks of pleuritic pain are not rarely the first symptom to attract

[1] Penna. Med. Jour., April, 1913.
[2] Wien. klin. Woch., 1913, xxvi, 1067.
[3] Adler: Primary Malignant Disease of the Lungs and Bronchi, 1912.

attention. Enlargement of the superficial veins of the chest and localized edema sometimes result from invasion of the anterior mediastinum and occlusion of large venous trunks. More rarely, hoarseness and dysphagia arise from pressure upon the recurrent laryngeal nerve and esophagus respectively. Enlargement of the lymph-nodes above the clavicle or in the arm-pit is an important symptom, but it is exceptional in sarcomatous cases. The temperature remains, as a rule, normal, but somewhat frequently in the later stages moderate fever of a remittent type supervenes and persists until the end. In 19 of 29 cases of carcinoma of the lung reported by Cottin[1] the temperature was above normal. Cachexia sooner or later develops in most cases, and is of importance in differentiating tumor from aneurysm.

**Physical Signs.**—In the absence of pleural effusion, percussion usually reveals an irregular area of dulness, gradually increasing in extent. If the bronchi in the affected region are pervious, auscultation elicits bronchial breathing and bronchophony. In the majority of cases, however, the bronchi are occluded, and, in consequence, both respiratory sounds and voice sounds are feeble or suppressed. When the root of the lung is involved and a main bronchus is partially obstructed the respiratory sounds over a limited area may be loud and stridulous. The chest wall over the tumor is sometimes distended, but it may be retracted if there are extensive pleuritic adhesions. In tumors attaining large dimensions the heart and abdominal organs are often considerably displaced. In a case of sarcoma of the thorax cited by Rolleston[2] the liver was so depressed that its lower border was on a level with the umbilicus.

In a large percentage of cases symptoms of pleurisy with effusion are the obtrusive features. If the fluid is not bloody at first it usually becomes decidedly so after two or three tappings. Microscopic examination of the sediment sometimes affords a diagnostic clue. A large number of cells exhibiting numerous mitoses, especially asymmetrical division forms, is in favor of malignancy (Rieder, Warthin, Dock). Rapid recurrence of the effusion after paracentesis is the rule.

The roentgen ray is often a valuable aid in diagnosis. The usual finding in tumor of the lung is the presence of one or more areas of increased density, homogeneous or slightly mottled, and surrounded by a hazy shadow of inflammatory reaction. The mediastinal density shows little or no change. In metastatic malignancy, according to Moore and Carman,[3] the areas of density are rounded, sharply circumscribed, homogeneous and without shadow zones of congestion. In cases with pleural effusion the roentgen examination should be made after thoracentesis. In tumors at the hilus bronchoscopic examination may also help in diagnosis.

The duration of intrathoracic malignant disease varies from a few weeks to two or three years.

**Diagnosis.**—This is often difficult. The presence of malignant disease elsewhere in the body or the history of an operation for a primary lesion is, of course, an important clue in secondary tumors. Occasionally, however, the symptoms of a metastatic growth so dominate the clinical picture that the primary lesion escapes recognition.

In cases of primary tumor marked by consolidation of the lung, suspicion may be aroused by certain anomalies in the clinical picture, as the unusual location or distribution of the dull area, the disproportion between the intensity of the dyspnea and the degree of development of the physical signs, or the constant presence of blood in the sputum without tubercle

[1] Annales de Méd., 1920, No. 6.
[2] Rolleston: Diseases of the Liver, 1905, p. 19.
[3] Amer. Jour. Roent., 1916, iii, 126.

bacilli. The fact must not be forgotten, however, that tuberculosis and malignant disease of the lungs not rarely coexist. Tuberculosis was present in 13 of 31 cases of malignant disease of the lungs reported by Wolff,[1] in 3 of 10 cases reported by Schwalbe,[1] in 2 of 60 cases reported by Ross[2] and in 6 of 29 cases reported by Cottin.[3] In rare instances the examination of scraps of tissue found in the sputum affords decisive information. Symptoms pointing to stenosis of the air passages, while not peculiar to tumor of the lung, are important. When pleural effusion is present, the character of the fluid, its rapid return after thoracentesis and the cytologic findings are sometimes suggestive. Too much importance, however, should not be attached to the occurrence of a slightly bloody exudate, since this is not uncommon in tuberculous pleurisy and pleurisy complicating chronic nephritis and other wasting diseases.

*Pulmonary syphiloma* may produce signs closely resembling tuberculosis on the one hand or malignant disease on the other. In the absence of any positive evidence of tuberculosis or malignant disease, a positive Wassermann reaction should be regarded as an indication for recourse to specific treatment. *Echinococcus disease of the lung* and *dermoid cyst* may yield most of the symptoms of malignant growth, although both are even more rare than the latter. Of 1816 cases of echinococcus disease occurring in the United States and collected by Sommer[4] the lung or pleura was involved in 147. Apart from the presence of cysts elsewhere, the expectoration of hydatid membrane, and the data afforded by thoracentesis, there are no characteristis signs. Presumptive evidence, however, might be forthcoming in the presence of pronounced eosinophilia and the fixation of complement in the hemolytic test. Exploratory puncture is not without danger, owing to the grave toxemia which may follow absorption of the hydatid fluid. Maydl[5] reports 11 cases of intrathoracic echinococcus disease in which a fatal result followed thoracentesis.

In the case of *intrathoracic dermoid* cyst the coughing up of hair or sebaceous matter is the only pathognomonic symptom. According to Shaw and Williams[6] this was observed in 7 of the 35 authentic cases reported in the literature up to 1905.

*Aortic aneurysm* can usually be differentiated by evidences of lues and by the increased mediastinal density and pulsating mass on roentgen examination. In *Hodgkin's disease* glandular enlargements are often found elsewhere, and roentgen examinations usually show bilateral and well circumscribed areas of density limited to the mediastinum.

**Treatment.**—Except in rare instances, the treatment of tumors of the lungs or pleura can only be palliative. In a case reported by Lenhartz the patient survived a lobectomy for 18 months.

## PLEURISY

**(Pleuritis)**

Inflammation of the pleura is a common disease. It may be primary or secondary. The former, however, is comparatively rare, the vast majority

[1] Fortsch. d. Med., 1895, xiii.
[2] Deutsch. med. Woch., 1896, xii.
Edinb. Med. Jour., Dec., 1914.
[3] *Loc. cit.*
[4] New York Med. Jour., Aug. 22, 1896.
[5] Ueber Echinok. der Pleura., Wien, 1891.
[6] Lancet, Nov. 4, 1905.

of cases being secondary to a morbid process in one of the adjacent organs, especially the lung, or to a general infection. The inflammation may be limited to a portion of the serous membrane (*circumscribed pleurisy*) or may involve its entire surface (*diffuse pleurisy*). According to the character of the inflammatory exudate pleurisy is designated *fibrinous or plastic, sero-fibrinous, or purulent* (empyema). The terms *acute* and *chronic pleurisy* are also used to indicate the course and duration of the disease.

**Etiology.**—Pleurisy is probably always infectious. Most of the cases occurring in apparently healthy persons follow exposure to cold, but it is likely that the chilling acts mainly by lessening the resistance of the serous membrane to infection. Recent investigations have shown that a large proportion of these so-called idiopathic cases are in reality of tuberculous origin. Thus, of 1541 cases of sero-fibrinous pleurisy collected from various sources, no less than 24.4 per cent. subsequently developed definite tuberculous lesions, and of 2,123 cases of pulmonary tuberculosis analyzed by Allard and Köster[1] there was an antecedent history of pleurisy in 650, or in 30 per cent. In an analysis of 5895 cases of pulmonary tuberculosis at the Phipps Institute it was found that 23.8 gave such a history.[2] Animal inoculations show still more clearly the close relationship between the two diseases. In this way 65.2 per cent. of 23 cases of sero-fibrinous pleurisy studied by Eichhorst[3] and 86 per cent. of 55 cases studied by Le Damany[4] were proved to be tuberculous. The immediate source of the infection in tuberculous pleurisy is not always apparent. Very often a small tuberculous focus is present in the lung. In other cases the pleura is probably involved from the bronchial lymph-nodes. Occasionally pleurisy in an otherwise healthy individual is of pneumococcic origin, the pleura instead of the lung bearing the brunt of the infection.

Trauma, without necessarily causing any wound of the thoracic wall, may set up pleurisy, probably not directly, however, but by creating a *locus minoris resistentiæ*. Not a few of the cases attributed to mechanical injury turn out to be tuberculous.

Involvement of the pleura by extension of disease from adjacent structures is of frequent occurrence. Thus, in pneumonia and tuberculosis of the lung pleurisy is almost invariably present. In many of these cases the exudate is fibrinous and not very abundant, but not uncommonly it is serous or purulent and copious. Pleurisy may also follow an extension of disease from the ribs, vertebræ, mediastinal lymph-nodes, esophagus, or even one of the abdominal organs, such as the stomach, liver, appendix, or Fallopian tube.

Inflammation of the pleura is not an unusual complication in various systemic infections, such as pyemia, septicemia, rheumatism, typhoid fever, influenza and scarlatina. Pleurisy in typhoid fever is usually produced by a superadded infection, but occasionally it is caused by the typhoid bacillus itself. In a few instances the typhoid bacillus appears to have caused no localized lesions except in the pleura. According to Sears[5] of 40 cases of typhoid pleurisy that were aspirated 17 were purulent, 16 serous and 7 hemorrhagic.

Pleurisy, like pericarditis and endocarditis, sometimes develops as a terminal infection in chronic nephritis, arteriosclerosis and other protracted diseases which profoundly disturb nutrition. The course of these cases may be either acute or chronic.

[1] Hygiea, Oct., 1911.
[2] Norris and Landis: Diseases of the Chest, Second Edit., p. 573.
[3] Corres.-Bl. f. schw. Aerzte, 1895, No. 10.
[4] La Presse Méd., Nov. 24, 1897.
[5] Boston Med. and Surg. Jour., Dec. 4, 1902.

The disease attacks persons of all ages, even the new-born. In adults, it is more common in males than in females. In children under 2 years of age pleurisy is almost always of the purulent variety.

**Bacteriology.**—As has already been stated, a large majority of the cases of sero-fibrinous pleurisy in apparently healthy adults are due to infection with the tubercle bacillus. Failure to demonstrate bacteria in the exudate by microscopic examination or cultural tests does not exclude tuberculosis; on the contrary it is strong presumptive evidence that a pleurisy has this origin. Positive results are very often obtained when such seemingly sterile exudates are injected into the peritoneal cavity of guinea-pigs. In experimenting, however, not less than 20 mils of the effusion should be injected. Purulent pleurisy, on the other hand, is not usually tuberculous. In adults, probably not more than 10 per cent. of the cases are of this nature, and in children the proportion is very much less. Of Blaker's[1] 81 cases of empyema in children only 3 were tuberculous. Even sero-fibrinous pleurisy in children does not seem to stand in such close relationship to tuberculosis as it does in adults. Purulent effusions that are apparently sterile are usually of tuberculous origin.

As an etiologic factor the pneumococcus ranks next in importance to the tubercle bacillus. Pneumococcus pleurisy is usually purulent, although it may be sero-fibrinous. At least 75 per cent. of the empyemas of children are due to pneumococci.

The streptococcus is also a relatively common cause of pleurisy, especially of empyema in adults. In the large majority of cases the organism emanates from a focus of streptococcic infection in the lung, or some other adjacent structure. In the streptococcic bronchopneumonia which prevailed in a number of the army cantonments in America during the winter of 1917–1918 the incidence of streptococcus empyema was from 30 to 40 per cent. which compares with an incidence of empyema of about 4 per cent. in ordinary pneumococcic pneumonia.

Other organisms are occasionally found in pleuritic exudates, either alone or associated with the pneumococcus or streptococcus; thus, the staphylococcus, typhoid bacillus, Friedländer's bacillus, colon bacillus, influenza bacillus, or diphtheria bacillus may be detected.

**Morbid Anatomy.**—At the outset the pleura loses its smooth and glistening appearance and becomes slightly roughened, dull, and injected. These changes are rapidly followed by the appearance of an exudate, which may be fibrinous, serofibrinous or purulent.

In *fibrinous pleurisy* the surface of the pleura, over a large or small area, is covered with grayish or yellowish membrane of variable thickness. When recent this deposit is friable and readily peeled off. Except in mild attacks the pleura usually is not restored to its normal condition; instead, organization of the exudate ensues, and in consequence the opposing surfaces ultimately become more or less closely knit by fibrous adhesions.

In *serofibrinous pleurisy* there is in addition to the deposit of fibrin a more or less abundant exudation of serum. The latter is usually of a pale yellow or yellowish-green color, and is frequently cloudy from the presence of loose particles of fibrin. Sometimes it is dark red from admixture with blood (*hemorrhagic pleurisy*); and occasionally, especially in tuberculous pleurisy, it is milky, this appearance being usually due to fatty granules from degenerated cells (chyliform fluid). The fluid presents the usual characteristics of inflammatory serum. It has a specific gravity averaging 1.020, and contains from 4 to 5 per cent. of albumin. On standing it often coagulates

[1] Brit. Med. Jour., May 23, 1903.

spontaneously. The amount of liquid ranges from a few cubic centimeters to several liters.

The lung in contact with the fluid is always rendered atelectatic to a variable depth, and in many cases the whole viscus is pushed upward and backward, the mediastinal structures, particularly the heart and large vessels, are forced toward the unaffected side, and the diaphragm is depressed, the liver or the spleen, in consequence, being displaced downward according as the effusion is on the right or the left side. In very large effusions the lung is found as a small mass of bluish airless tissue in the upper part of the thorax, close to the spine. Occasionally the condition of atelectasis becomes permanent, the compressed lung ultimately undergoing a fibroid change. This result is not likely to be observed, however, unless the effusion persists for a long time and the compressed lung is bound to the chest wall by extensive adhesions. On the uninvolved side the lung shows compensatory inflation.

*Purulent pleurisy* or *empyema* may begin with the formation of pus, or it may follow a serofibrinous pleurisy, the liquid exudate in the latter being gradually transformed into pus. The effusion is thin and merely turbid when it contains comparatively few leucocytes, but thick and creamy when it is very rich in corpuscles. In pneumococcic infections thick, creamy effusions are the rule; in streptococcic infections the exudate is commonly thin and dirty looking. A variable amount of fibrin is usually found floating in the pus and attached to the surface of the pleura. Sedimentation of the formed elements not infrequently occurs, fairly clear liquid rising to the top, and dense granular or flocculent matter falling to the bottom of the cavity. This tendency of purulent effusions to separate into layers has a practical bearing, inasmuch as aspiration at one level of the chest occasionally reveals serum and at another level pus.

In some cases, owing to the entrance of saprophytic bacteria into the pleural sac, the pus undergoes decomposition and acquires an extremely fetid, disgusting odor (*putrid empyema*) and very rarely, in consequence of infection of the exudate by gas-forming bacilli, an empyema becomes transformed into a pyo-pneumothorax without rupturing the pleura.

In many cases of pleurisy, especially of empyema, the subpleural lymphatics become infiltrated with round cells, the inflammatory process extending well into the lung. In this way a *pleurogenous interstitial pneumonia*, suppurative or fibroid, according to the intensity of the infection, is sometimes produced. In like manner, too, inflammatory and degenerative changes are not infrequently set up in the intercostal muscles and diaphragm (Rohrer, Coplin). Empyema, particularly in children, is not rarely associated with purulent pericarditis, mediastinitis or peritonitis.

**Symptoms of Fibrinous or Plastic Pleurisy.**—This form of pleurisy is usually attended by a stitch-like pain in the side, short, dry cough, more or less dyspnea and slight fever. The chief diagnostic feature, however, is the friction sound. This is usually heard during inspiration, especially at the end of the act, although it may be heard also during expiration. It has a peculiar rubbing or creaking character, and is often jerky or interrupted. It seems very close to the ear and is intensified by pressure. Occasionally it is audible to the patient. In some cases a to-and-fro rub, corresponding to the sound, is perceptible on palpation. When the pain is severe there may be decided impairment of the respiratory movements and weakening of the breath sounds upon the affected side.

Many cases of fibrinous pleurisy run an entirely latent course. This is shown in the great frequency with which the constant sequels of the disease—

thickening and adhesion of the pleural membranes—are found post mortem. Permanent pleural thickening (*chronic dry pleurisy*) is sometimes discovered accidentally during life in routine physical examination, being revealed by the following signs: Diminution of respiratory movement, absence of Litten's diaphragm phenomenon,[1] impairment of tactile fremitus, slight dulness on percussion, and weakening of the breath sounds.

**Symptoms of Serofibrinous Pleurisy.**—The mode of onset is extremely variable. In many cases the disease is ushered in with chilliness and a more or less intense stabbing pain in the affected side. This pain is aggravated by movement, especially deep breathing, coughing, or stooping, and is often attended with tenderness on pressure. In some instances, especially in children, it is referred to the abdomen, and thus strongly suggests appendicitis or perforative peritonitis. Occasionally the pains are quite general and simulate those of rheumatism. In other cases the invasion is like that of lobar pneumonia, a severe chill accompanying the characteristic stitch in the side. In a third group of cases the disease develops slowly and painlessly, the first symptoms to attract attention being general malaise, loss of appetite, increasing weakness, and slight dyspnea on exertion. Not infrequently the process is so latent that the patient continues at work for some time, even though his chest contains a large quantity of liquid.

Irrespective of the mode of onset, fever is generally present, at least in the early stages. The temperature, however, does not run a typical course, and, as a rule, does not exceed 103° F. In many cases it ends by lysis in from one to two weeks, but it may continue for a much longer period. In debilitated individuals the disease may be virtually afebrile. The pulse range is from 90 to 120, according to the temperature. In rare instances there is an inspiratory diminution of the pulse (*pulsus paradoxus*). At first the respirations are hurried and shallow on account of the pain; later, there may be, decided, even urgent, dyspnea from the pressure of the effusion on the lung, intercostal muscles and diaphragm. Generally speaking, the more rapidly the effusion forms, the more severe is the dyspnea. In subacute cases there is often little or no dyspnea so long as the patient remains quiet. Cough is usually present. Sometimes it occurs only when the patient takes a deep breath or changes his position. At first it is short, smothered and painful; after the development of effusion it is usually more frequent but less distressing. Occasionally there is complete absence of cough. In uncomplicated cases, expectoration is entirely wanting, or it is scanty and consists merely of frothy mucus.

**Physical Signs.**—At the onset serofibrinous pleurisy usually presents the same objective evidence as fibrinous or plastic pleurisy, that is a superficial, jerky friction sound, with, perhaps, a diminution of the respiratory movements on the affected side as a result of pain. After the development of liquid effusion the physical signs are as follows:

*Inspection.*—The respiratory excursion is deficient or absent on the affected side, and is exaggerated on the healthy side. If the effusion is copious the eye may detect unilateral distention of the chest and obliteration of the intercostal depressions. Litten's phenomenon is absent. Displacement of the heart is an important feature. In left-sided effusions the apex-

[1] If a healthy person is placed in a horizontal position with the feet toward the window and all cross-lights are excluded a narrow shadow may be seen descending between the sixth and the ninth ribs in each axilla during full inspiration. It is due to the separation of the diaphragmatic pleura from the costal pleura and the falling inward of the intercostal tissue during the inspiratory descent of the diaphragm. The shadow is usually annuled by pleural effusions, pneumonia and pleuritic adhesions but not affected by enlargements of the liver and subphrenic abscesses.

beat may be invisible or be found to the right of the sternum, and in right sided effusions it may be pushed outward considerably beyond the left nipple. Patients frequently lie on the affected side, so that the expansion of the sound lung may be as free as possible, but this posture is by no means constant.

Dilatation of the pupil on the side of the pleurisy is occasionally observed and is probably caused by irritation of the thoracic sympathetic.

*Palpation.*—The vocal fremitus is almost always absent or much diminished over the effusion and exaggerated above it. In this connection, it should be remembered that fremitus is normally stronger upon the right side than upon the left side. Occasionally, a very considerable effusion, especially in children, fails to annul the fremitus. This anomaly is difficult of explanation. It is supposed, however, that the vibrations of the voice are transmitted from the compressed lung through bands of adhesions to the chest wall, or that the chest wall itself acts as the conductor.

In very rare instances a massive effusion results in inversion of the diaphragm on the affected side and the production of a tense, rounded, immobile mass in the upper part of the abdomen (Riesman,[1] Funk[2]).

*Percussion.*—An area of dulness or flatness corresponding roughly to the volume and position of the fluid is constantly present. The dulness begins usually posteriorly, and as the effusion increases it extends upward and laterally and then anteriorly. In left-sided pleurisy the semilunar tympanitic space above the costal border and between the liver and spleen (*Traube's space*) is generally obliterated, even when the exudation is slight. In moderate effusions without adhesions, when the patient is in the sitting or erect posture, the upper border of dulness is not horizontal, but is highest in the posterior axillary line, from which point it bends forward to the sternum and backward to the vertebral column, forming an irregular parabola (Damoiseau[3]) or, more frequently, the S-shaped curve described by Ellis.[4] To Garland[5] belongs the credit of demonstrating that the factor in preventing the fluid from assuming a hydrostatic level is the retractile or lifting force of the lung, which is apparently greater in the axillary region than at other points. A change in the upper limit of dulness on changing the position of the body is sometimes demonstrable in moderate effusions and is very significant. In testing for this mobility comparisons should not be made too quickly, as two or three minutes are sometimes required for the fluid to shift. Except in very small effusions the feeling of resistance on percussion is much more marked over a pleural effusion than it is over an ordinary pneumonic solidification.

Above the line of dulness the note is hyper-resonant or tympanitic—Skoda's resonance. Sometimes the pitch of this note changes as the patient opens and closes his mouth (Williams' tracheal tone), and occasionally a typical cracked-pot sound may be obtained. With the patient in the sitting posture a small right-angled triangle of dulness is usually found along the spine on the side opposite the effusion (Grocco's sign[6]). The vertical side of this triangle is represented by a line extending along the mid-spine from the upper limit of flatness on the affected side; the base, by a line following the lower limit of pulmonary resonance on the healthy side for a distance of from 3 to 6 cm., and the hypotheneuse, by a line joining the extremities of the

[1] Amer. Jour. Med. Sci., 1920, clix, 353.
[2] Med. Clin. of North America, Jan., 1921.
[3] Archiv. gén. de Med., Oct., 1843.
[4] Boston Med. and Surg. Jour., Jan. 1, 1873.
[5] Boston Med. and Surg. Jour., Jan. 23, 1874.
[6] Riv. crit. di Clin. Med., Firenze, 1902, iii, 274.

other two lines. Grocco's sign is of some value in the diagnosis of pleural effusion, but it is not pathognomonic. It is sometimes present in pneumonia, in abdominal effusions and tumors, and in pregnancy. It probably depends in part upon a displacement of the posterior mediastinal contents toward the sound side and in part upon a damping of vibrations by the effusion.

Lastly, percussion also serves to demonstrate displacement of the adjacent organs, especially the heart and liver.

*Auscultation.*—In the majority of cases as the fluid accumulates the respiratory murmur becomes more and more feeble and distant, and finally disappears altogether. Absence of breath sounds, however, is by no means constant. Not infrequently, even when the quantity of fluid is very large, bronchial breathing is heard all over the region of dulness. As a rule, the bronchial breathing of pleural effusion is soft and distant, but sometimes, especially in young children, it is as harsh and intense, as in pneumonia.

The voice sounds usually correspond with the breath sounds; that is, they are absent when the respiratory sounds are suppressed and intensified when the breathing is loud and bronchial. Egophony, a modification of bronchophony in which the voice sounds have a nasal or bleating character, is frequently heard in the neighborhood of the inferior angle of the scapula in medium-sized effusions. This phenomenon probably depends, as Stone[1] suggests, upon the power of the fluid to arrest the fundamental tones of the voice, while allowing the overtones to pass. Bacelli's dictum that the whispered voice is transmitted through serous but not through purulent exudations is not supported by clinical evidence.

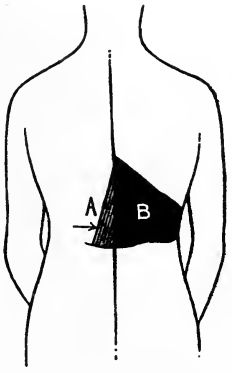


FIG. 16.—A, Grocco's triangle of dulness; B, dulness of pleural effusion.

Ordinarily, the friction sound is suppressed in the stage of effusion, or is audible only at the upper border of the liquid; occasionally, however, it may be heard directly over the dull area. When this is the case, it is likely that the two pleural surfaces are still in apposition at certain points.

*Roentgenologic Examination.*—In the majority of cases of serofibrinous pleurisy, fluoroscopic and roentgenographic studies do not add materially to the information obtained by percussion and auscultation. They may prove very helpful, however, when emphysema is present or when the effusion is loculated. Ordinary liquid accumulations produce a well-defined shadow in the dependent part of the pleural sac. The upper margin of the shadow is usually irregularly curved and may change with the position of the patient. Very dense shadows are suggestive of empyema. In addition to the shadow of the effusion, the x-ray also shows very clearly the displacement of the heart, mediastinum and diaphragm.

The stage of absorption is marked by a gradual disappearance of the dulness and return of the normal fremitus and breath sounds. At this period, also, the fricton sound may again become audible. This redux friction, which is usually louder and coarser than the primary rub, often remains for several days or weeks. Even in cases in which complete recovery

[1] St. Thomas' Hosp. Reps., 1871, Vol. II.

ultimately occurs, many weeks or months may elapse before all evidence of the disease disappears. Very often resolution is only partial; the liquid exudate is absorbed but the pleural layers are left permanently thickened and perhaps adherent. In these cases the expansion, tactile fremitus, percussion resonance, and respiratory murmur remain defective, and the side of the chest sometimes becomes more or less flattened and retracted.

**Symptoms of Purulent Pleurisy or Empyema.**—Purulent pleurisy may begin as a suppurative process or as an ordinary serofibrinous inflammation. The general symptoms and physical signs are much the same as in sero-fibrinous pleurisy, but in addition there is usually evidence of septic infection—irregular fever with abrupt exacerbations and remissions, chills, copious sweats, and increasing pallor. In contrast with sero-fibrinous pleurisy there is commonly a well marked polymorphonuclear leucocytosis, the count ranging from 15,000 to 45,000. Distention of the chest, bulging of the intercostal spaces, and displacement of the heart are more pronounced, as a rule, in empyema than in sero-fibrinous pleurisy. Not rarely there is slight edema of the chest wall on the affected side, although this is not absolutely indicative of suppuration. A circumscribed swelling having the characteristics of an ordinary abscess appears on the surface of the chest when discharge of the pus through the skin is imminent (*empyema necessitatis*). In rare instances a systolic pulsation, localized or diffuse, is observed on the affected side. This phenomenon is almost always indicative of pus (see p. 619). Clubbing of the fingers is not uncommon in empyema. Although usually a late manifestation, it may appear as early as the third or fourth week.

In many cases of empyema, owing to an entire absence of septic manifestations, exploratory puncture affords the only means of deciding with certainty as to the nature of the fluid. In applying this test it is advisable to use a needle of moderate size since thick pus cannot be drawn through a fine one.

**Special Forms of Pleurisy.** *Double Pleurisy.*—In exceptional cases pleurisy occurs on both sides at the same time. Double serofibrinous pleurisy is usually due to tuberculosis, while double empyema is usually the result of pneumonia. Of Blaker's[1] 81 cases of empyemata in children, 9 were bilateral, but Koplik[2] observed a bilateral involvement in only 3 of 170 cases of empyema in children. The physical signs are the same as in unilateral pleurisy. The prognosis is always of considerable gravity, but not absolutely unfavorable.

*Hemorrhagic Pleurisy.*—All pleuritic effusions contain a certain number of red blood corpuscles, but they are not designated as hemorrhagic unless blood is present in sufficient quantity to be recognized by the unaided eye. Hemorrhagic pleurisy is usually the result of tuberculosis or of malignant disease of the lung or pleura, but it sometimes occurs in the later stages of such debilitating conditions as alcoholism, chronic nephritis, cirrhosis of the liver, leukemia and scurvy. Occasionally it is met with in persons who appear to be otherwise in perfect health. The source of the effused blood is the engorged capillaries of the pleura itself or the newly-formed vessels which ramify in the fibrinous exudation.

*Diaphragmatic Pleurisy.*—Occasionally, the serous lining of the upper surface of the diaphragm is the only portion of the pleura involved. This form of pleurisy is usually fibrinous, but it may be serous or purulent. It is characterized by severe pain, which is felt not directly over the seat of the inflammation, but in areas supplied by the somatic nerves emanating from

[1] *Loc. cit.*

[2] Diseases of Infancy and Childhood, 1910, 652.

those segments of the spinal cord which receive the sensory nerves of the diaphragmatic pleura (lower six intercostal nerves) and of the diaphragm itself (phrenic nerve). Thus, in 61 cases analyzed by Capps[1] the pain was referred to the abdomen, especially an upper quadrant, in 54 and to the neck, especially the trapezius ridge, or to the cap of the shoulder in 33. The pain is usually induced or aggravated by cough and deep breathing, and in the majority of cases it is accompanied by superficial hyperesthesia and points of tenderness. Deep pressure over the seat of the abdominal pain, however, is well borne, which is in contrast with what is observed in cases of cholecystitis, appendicitis, etc. Vomiting is not uncommon, and occasionally there is persistent hiccough. Cough is present, as a rule, and dyspnea is often pronounced. The respiratory movements at the base of the chest and Litten's diaphragm phenomenon are usually absent. The upper part of the rectus on one side, however, may be energetically contracted during inspiration. Percussion and auscultation commonly yield negative results, although friction sounds are occasionally audible in the region of the diaphragm.

The detection of fluid between the lung and the diaphragm is greatly facilitated by x-ray examinations. Suggestive findings are a shadow in the dependent portion of the thorax with flattening and immobility of the diaphragm. In subphrenic collections of fluid the diaphragm is also fixed, but it is elevated and its contour is preserved.

*Encapsulated Pleurisy.*—A pleurisy is said to be encapsulated or loculated when the effusion is confined to relatively small sacs or pockets by adhesions. Any part of the pleural cavity may be affected. A favorite site is at the base of the lung posteriorly. In some cases the encysted effusion is between two lobes of the lung (interlobar pleurisy) and in others it is between the under surface of the lung and the diaphragm. As a rule, encapsulated effusions are purulent. In many instances a loculated empyema is in communication with the lung, a subpleural abscess having originated the empyema or the latter having first formed and then invaded the lung. Not rarely the symptoms are definite and the localization of the pus is readily revealed by the usual signs of a pleural effusion in a circumscribed area of the chest. In many cases, however, although an encapsulated empyema is suspected from the persistence of symptoms after an attack of pneumonia or of ordinary pleurisy, it is difficult or impossible to locate the pus by physical signs or even exploratory puncture. Under these circumstances the x-ray may render invaluable aid. Occasionally the site of the empyema is suggested by a circumscribed area of edema or by localized tenderness on very firm pressure. If all means of localization fail and the symptoms point indubitably to pus, exploratory thoracotomy should be undertaken.

*Pulsating Pleurisy.*—This comparatively rare condition has been known since the seventeenth century, but it was first described accurately by Bérard in 1810. The effusion is almost always purulent (pulsating empyema) and on the left side. Of 95 cases analyzed by Sailer[2] in only 12 was the effusion non-purulent, and in only 6.4 per cent. of the 110 cases of pulsating pleurisy collected by Levi[3] was the effusion on the right side. The pulsation, which is almost always systolic, may be circumscribed or diffuse. In more than one-third of the recorded cases it has been associated with empyema necessitatis. Occasionally two or three pulsating projections are present. The chief factors concerned in producing the pulsation appear to

[1] Amer. Jour. Med. Sci., Mar., 1916, 333.
[2] Amer. Jour. of Med. Sci., Aug., 1904.
[3] Centralbl. f. d. Grenzgebiete d. med. u. chir., 1914, No. 3, xviii.

be a certain degree of tension of the liquid, rigidity of the mediastinal tissues and diaphragm, atelectasis or encapsulation of the lung, and relaxation of the thoracic wall, such as occurs especially in empyemas of necessity.

**Diagnosis of Pleurisy.**—Ordinary cases of pleurisy are easily recognized. The stitch-like pain in the side, comparatively mild fever, short dry cough, rapid respiration, grating friction-sound, and, later, the pronounced dulness, displacement of the adjacent organs, and diminution of fremitus, respiratory sounds and voice sounds leave little room for doubt. In *pneumonia*, as a rule, the temperature is higher, the dyspnea is more urgent, and the expectoration is accompanied by tenacious rusty sputa. In both pneumonia and pleurisy the affected side shows some degree of immobility and becomes dull on percussion, but in pneumonia the intercostal spaces are not obliterated, the heart is not displaced, the dulness is rarely so absolute, or the resistance to the finger, as a pleximeter, so great, the vocal fremitus is increased, and the breath sounds are, as a rule, loud and bronchial. It must not be forgotten, however, that a pneumonic consolidation may present nearly all the signs of an effusion, that an effusion, especially in children, may present nearly all the signs of a pneumonic consolidation, and that the two diseases may coexist. In such cases an exploratory puncture may afford the only means of arriving at a positive diagnosis.

*Pleurodynia* is distinguished from pleurisy by the absence of fever and friction sounds. In *intercostal neuralgia* the pain is usually paroxysmal, there are tender points along the course of the affected nerve, fever is absent, and so are friction sounds.

A pleural friction sound is not likely to be mistaken for a *pericardial friction sound* unless that part of the pleura is involved which overlaps the heart. When this is the case the sounds are often indistinguishable. Pleurisy may be suspected, however, if the friction sound decreases in intensity when the breath is held during expiration. An encapsulated pleural effusion near the left border of the heart sometimes closely simulates a *pericardial effusion*, but as a rule the dull area extends further to the left and downward, the dyspnea is less pronounced, the heart sounds are less muffled, and the pulse is less disturbed than in pericarditis.

*Hydrothorax* yields the same physical signs as an inflammatory effusion, and, although it is more commonly bilateral than the latter, it is frequently unilateral, especially in chronic heart disease. In hydrothorax, however, there are usually other manifestations of the primary disease that has caused the effusion, and pain, fever, friction sounds, etc. are absent. Moreover, in hydrothorax the fluid, as a rule, has a specific gravity below 1.015 and often shows an excess of endothelial cells in sheets or plaques, rather than a predominance of lymphocytes or polymorphonuclear cells.

Among other conditions that sometimes simulate pleuritic effusions may be mentioned pulmonary atelectasis, tumor of the lung, echinococcus of the pleura or liver, abscess of the liver, and subphrenic abscess.

Exploratory puncture is the only certain means of determining the *nature of the pleuritic effusion*, although the presence of pus is frequently suggested by the symptoms of sepsis. The *etiologic relations of the disease* may usually be determined by the clinical history and a bacteriologic examination of the exudate. A sterile effusion is strongly suggestive of tuberculosis. Very frequently exudates that are apparently sterile when examined in the ordinary way will be found to contain tubercle bacilli when examined by the Löffler method or that of Jousset.[1] Briefly, Jousset's method consists in allowing the fluid to coagulate, digesting the clot with artificial gas-

[1] Arch. de méd. expér., vol. xv, 1903.

tric juice, centrifugalizing the digested material, and making cover-slip preparations from the precipitate. Cytodiagnosis, or the differential enumeration of the cells of the exudate, is easily practiced, and also affords a fairly reliable means of determining the etiology of serous pleurisy. A predominance of lymphocytes in stained preparations of the sediment points to tuberculosis, but it must be borne in mind that an excess of lymphocytes is occasionally found in non-tuberculous exudates and that in the early stages of tuberculous pleurisy there may be for a short period an increase of polymorphonuclear cells. A large number of polymorphonuclear forms, however, is strongly suggestive of infection with pneumococci, streptococci or other pyogenic organisms. According to O. H. P. Pepper[1] the effusion of typhoid pleurisy is characterized by numerous discrete endothelial cells, many of which show active phagocytosis. In pleural effusion of the mechanical type endothelial cells are also in the majority, but they are rarely numerous, frequently occur in groups or plaques of two or more, and seldom display phagocytic properties.

Finally, in doubtful cases, recourse may be had to the tuberculin test or to animal inoculation to confirm or exclude the tuberculous nature of the disease.

**Prognosis, Course and Events.**—The prognosis depends mainly upon the cause of the disease and the character of the exudate. In cases of fibrinous or serofibrinous pleurisy, when there is no serious underlying disease, the immediate outlook is good. The natural termination of such cases is recovery of the patient, with perhaps some thickening of the pleura and adhesions. Complete restoration of the pleura may occur if only a small amount of fibrin is present. In serofibrinous pleurisy absorption often occurs spontaneously in from a few weeks to a few months. In rare instances, even when the effusion is not excessive, sudden death occurs, an accident which is usually caused by thrombosis of the pulmonary artery or heart and subsequent pulmonary embolism and infarction, although it may be due to pulmonary edema, to syncope, or, according to some authors, to kinking of the aorta or vena cava through displacement of the heart by the effusion.

While spontaneous absorption is of frequent occurrence in sero-fibrinous pleurisy, it sometimes fails. In this event the effusion may become purulent, or it may remain for months, or even years, without special change (*chronic serofibrinous pleurisy*).

Considerable caution must be exercised in predicting the ultimate outcome of pleurisy with effusion, since many patients with the disease later develop tuberculosis.

In uncomplicated pneumococcic empyema the prognosis, while more doubtful than that of sero-fibrinous pleurisy, is on the whole favorable if the sac be promptly opened and drained. The average mortality in adults is probably about 10 per cent. In children more than 5 or 6 years of age the prospects are even better than in adults. In infants under two years, however, the mortality is very high, probably between 50 and 75 per cent. When the disease is allowed to take its normal course, it usually sooner or later proves fatal. Of course, complications, such as pericarditis, meningitis and peritonitis, render the outlook extremely gloomy under any circumstances. In streptococcic empyema the prognosis should always be made with considerable reserve, since in many of these cases death from sepsis eventually ensues, even after operative evacuation of the pus.

When left to itself the purulent exudate sometimes spontaneously ruptures the pleural sac. It may escape through the lung either by boring into

[1] Amer. Jour. Med. Sci., May, 1916.

the alveolar tissue, or by directly perforating into a bronchus. In the latter event pneumothorax almost inevitably follows. In very rare instances the discharge of pus into the bronchi takes place so suddenly that the patient is instantly suffocated. In other cases the empyema breaks through the chest wall (*empyema necessitatis*), the point of rupture usually being located in the fifth intercostal space below the nipple. Occasionally there are several fistulous openings. Rupture of the exudate externally, or even internally into the lung, is sometimes followed by complete recovery; as a rule, however, the sac refills again and again, until finally the patient dies of exhaustion, of metastatic abscesses in the brain, kidneys or other organs, or of amyloid degeneration of the viscera. In exceptional cases the pus breaks into the esophagus, pericardium or stomach or burrows to some remote point from the thorax. Spread of the infection to the abdomen is rare in comparison with the frequency with which subdiaphragmatic infection spreads to the pleura.

An empyema that remains intact usually kills through septicemia and exhaustion. Occasionally, however, absorption of the more liquid portion of the pus occurs and the residue becomes inspissated and in time infiltrated with calcium salts. Healing in purulent pleurisy is almost always accompanied by the formation of more or less scar tissue. Somewhat frequently, especially when the disease has lasted a long time, the pleural layers are left greatly thickened and universally adherent. In such cases there is a marked sinking in of one side of the chest, with dislocation of the heart and retraction of the lung. Ultimately even the spine may become twisted by the contracting cicatricial tissue.

**Treatment.**—The patient should be kept in bed and restricted to a liquid or semi-solid diet. Free catharsis should be maintained throughout the attack. Pain is often relieved by the application of hot fomentations, sinapisms or turpentine stupes. Strapping the affected side from mid-spine to mid-sternum with broad strips of adhesive plaster, as originally suggested by Frederick T. Roberts, is also useful. Morphin is sometimes necessary. For excessive pain, however, no measure is so uniformly efficient as the application of a few wet cups.

Acute cases of pleurisy in robust subjects are often favorably influenced by the administration of salicylates, a method of treatment, which has been especially advocated by Aufrecht, Fiedler, Dock, and others. From 1 to 1½ drams (4.0–6.0 gm.) of sodium salicylate should be given in the twenty-four hours, the dose being gradually reduced as the good effects become manifest. In asthenic, protracted cases of pleurisy the salicylates are of no avail and may prove harmful.

After the acute symptoms have subsided the indications are to accomplish the removal of the fluid, to maintain nutrition, and to secure complete expansion of the lung.

*Removal of Serous Effusion.*—Counterirritation by means of iodin or small ("flying") blisters sometimes appears to promote absorption. In vigorous subjects the administration of saline purgatives, according to the method suggested by Matthew Hay, may be tried, although it usually proves disappointing. The quantity of fluid consumed by the patient is restricted to a minimum, and every morning or every other morning from ½ to 1 ounce (15.0–30.0 gm.) of magnesium sulphate is given in concentrated solution an hour before breakfast. Diuretics (theobromin, caffein, potassium citrate) and potassium iodid have been recommended, but they are of questionable value, and the latter may prove harmful by disturbing digestion.

Autoserotherapy has some champions, but the author's experience with

it has not been very satisfactory. The method consists in reinjecting under the skin from 2 to 5 mils of the fluid aspirated from the pleural cavity. A sharp febrile reaction, accompanied by chill, often follows the injection.

While in many cases spontaneous absorption of the effusion eventually occurs, much saving of time is effected by early recourse to paracentesis. As a rule, this operation should not be delayed longer than ten days or two weeks if the effusion is considerable and shows no signs of receding. The presence of fever is not a contra-indication; indeed, the temperature frequently falls upon the removal of the fluid. Irrespective of the period of the disease paracentesis is demanded: (1) When there is sufficient fluid to induce marked dyspnea, cyanosis, persistent cough or other pressure symptoms; (2) when the fluid reaches the third rib, and there is much displacement of the adjacent organs. The suspected presence of pus is also, of course, always to be regarded as sufficient ground for operative intervention.

*Paracentesis Thoracis.*—The patient should be brought to the edge of the bed, placed in a semirecumbent position with the thorax inclined slightly toward the healthy side, and supported by an assistant. The most favorable site for the puncture is usually the fifth or sixth intercostal space in the mid-axillary line or the seventh intercostal space near the post-axillary line. Care should be taken that the needle is aseptic, that the patient's skin at the site of puncture and the hands of the operator are surgically clean, and that the apparatus is in perfect working order. Local anesthesia may be secured by means of a spray of ethyl chlorid. The needle should be inserted with a quick thrust along the upper margin of the rib, the depth of the puncture being gauged by the forefinger. As soon as a loss of resistance indicates that the point of the needle has entered the effusion, the valve opening into the aspirating jar should be opened and the stylet within the needle withdrawn. The needle having been introduced, the operator should satisfy himself that it is freely movable, should hold it in position throughout the operation, and as the evacuation proceeds should slowly raise the exposed end so as to keep the inner opening below the level of the fluid in the pleural sac. The aspiration should be effected slowly, and at intervals it should be stopped by compressing the conducting tube. Too rapid evacuation may excite engorgement of the lung and edema.

The amount of fluid which should be removed depends somewhat upon the size of the effusion and the ease with which it can be evacuated. Even with large effusions it is rarely advisable to withdraw more than a quart (1.0 L.). The removal of small quantities is in many cases followed by the rapid absorption of the remainder. Under no circumstances should extreme efforts be made to obtain the largest possible amount of fluid. The operation should be terminated at once if incessant cough, severe pain, dyspnea, palpitation, tendency to syncope, or other untoward symptoms appear.

When the requisite amount of fluid has been evacuated, the needle should be withdrawn quickly from the chest, and the puncture closed with gauze and collodion.

If the exudate reaccumulate, aspiration may be repeated after the lapse of a week or ten days. Free incision of the thoracic wall with thorough drainage has given good results in some cases in which the fluid has reaccumulated after repeated tappings.

Occasionally, attempts at aspiration are unsuccessful. The cause of failure may be plugging of the canula, great thickening of the pleura, or encapsulation of the effusion. Under these circumstances it may be necessary to make repeated trials before a flow can be established. The aspiration of pleural exudates is rarely attended by accidents of any kind. Sudden

death, the result of cerebral anemia, has been reported. Such an accident is not likely to occur if the evacuation be effected slowly and arrested immediately on the first appearance of any untoward symptom. Another grave and even fatal complication of thoracocentesis, but also very rare, is a peculiar form of pulmonary edema, which is manifested by cough, intense dyspnea, and profuse albuminous expectoration. According to Riesman, who has collected 32 cases from the literature, the principal cause of this condition seems to be either too rapid or too great a withdrawal of fluid.

*To Maintain Nutrition and Secure Normal Expansion of the Lung.*—Throughout the course of the disease the patient's strength should be conserved by rest, fresh air, and good food. During convalescence tonics, such as iron, strychnin, cod-liver oil, etc. may often be prescribed with advantage. Systematic respiratory exercises are of great value in favoring normal pulmonary expansion. The hygienic measures called for in early cases of pulmonary tuberculosis are also necessary after recovery from an attack of ordinary serofibrinous or fibrinous pleurisy.

*Empyema.*—The treatment of empyema is surgical. The indications are to evacuate the pus and to secure free drainage. If the effusion is merely cloudy and not distinctly purulent, thoracentesis may be tried and repeated once, with the understanding that surgical intervention will be required if the fluid continues to reaccumulate.

## PNEUMOTHORAX

**Etiology.**—1. Pneumothorax—the presence of air or gas in the pleural cavity—is caused in the vast majority of cases by *rupture of the visceral layer of the pleura* allowing air to escape from the lung. This may arise from direct injury, as by a stab wound or the penetration of the lung by a broken rib. Occasionally it results from a violent contusion or powerful muscular effort, the ribs and chest-wall remaining uninjured. Such an accident very rarely occurs in a paroxysm of whooping-cough. Far more frequently, the pulmonary pleura is perforated in the course of some disease affecting the lung, especially tuberculosis. *From 80 to 90 per cent. of all cases of pneumothorax are caused by the giving way of a cavity or the softening of a cheesy nodule on the surface of the lung.* The proportion of pronounced tuberculous cases in which pneumothorax develops is probably 5 or 6 per cent. Rupture of the pulmonary pleura may also occur in consequence of abscess or gangrene of the lung, pneumonia, emphysema, bronchiectasis, or even hemorrhagic infarction. In other cases the disease is produced by the spontaneous discharge of an empyema through the lung. This cause ranked next in importance to tuberculosis in the days when empyema was allowed to take its natural course. Occasionally, pneumothorax develops spontaneously or after moderate exertion in persons who are apparently healthy. Such cases probably depend upon localized emphysema or a very small tuberculous nodule. Recurrence of the pneumothorax has been observed in several instances. Gabb[1] cites a case in which there were four attacks with intervals of six, two and six years.

2. Less frequently pneumothorax results from *rupture of the parietal pleura.* This may be caused by a penetrating wound of the thoracic wall, the spontaneous or operative evacuation of an empyema, or the aspiration of the chest for fluid. As the intrathoracic pressure is persistently negative,

[1] Brit. Med. Jour., vol. xi, 1888.

one would suppose that an open wound of the chest would invariably allow free access of air to the pleural cavity, but such is not the case. Under favorable conditions the injury seems to be immediately followed by certain compensatory changes in the volume of the lung which prevent the pleural surfaces from separating. Sometimes, though very rarely, the air is derived from the alimentary canal, the parietal pleura being perforated by an ulcer or a cancer of the esophagus, stomach or bowel.

3. Finally, in a few instances a pneumothorax has supervened on a pyothorax *without perforation of the pleura* as the result of decomposition of the pus by a gas-producing organism such as the Bacillus aërogenes capsulatus or the Bacillus coli communis.

Pneumothorax is about four times as frequent in men as in women. More than half of the cases occur in the third and fourth decades. The disease is very rare in young children. Only 18 cases had been recorded in children up to the year 1903 (Bovaird[1]) and all but 3 of these were the result of causes other than tuberculosis, such as pneumonia, whooping cough, measles, etc.

**Morbid Anatomy.**—Ordinarily pneumothorax is unilateral. According to Rose[2] only 14 cases of bilateral pneumothorax had been reported up to 1899. One side is apparently affected about as often as the other. Of Drasche's series of 198 tuberculous cases[3] 109 (55 per cent.) were right-sided. When pleuritic adhesions are present or the lung is extensively solidified perforation of the pleura may produce only a *partial or circumscribed pneumothorax*, with comparatively little displacement of the adjacent structures. On the other hand, when there are no adhesions and the lung is capable of contracting, the entrance of air into the pleura usually results in what is termed a *diffuse or free pneumothorax*. In this condition the lung is completely collapsed and lies in the upper and posterior portion of the thorax, against the spine, the heart and mediastinum are drawn to the opposite side by the elastic traction of the healthy lung, the affected side of the chest is distended, and the diaphragm is depressed.

Weil has further divided the disease into open, valvular, and closed pneumothorax. In *open pneumothorax* the air has free entrance and exit through the perforation; consequently the pressure within the pleural cavity becomes equal to that of the atmospheric air. In *valvular pneumothorax* the opening is of such a character that air enters the pleural cavity during inspiration but cannot be expelled during expiration. Under these circumstances the intrapleural pressure may exceed that of the atmospheric air. A *closed pneumothorax* is one in which the fistulous opening has become sealed and communication with the outside air no longer exists. Pure pneumothorax is rare. The pleura, even when previously healthy, very seldom escapes infection at the time of the perforation; hence in the vast majority of cases the air is associated with more or less liquid effusion. According as the latter is serous or purulent, the condition is known as *hydropneumothorax* or *pyopneumothorax*. Occasionally, when the disease is caused by the rupture of an emphysematous bleb no effusion is found and the air is quickly absorbed.

**Symptoms.**—Circumscribed pneumothorax, especially when occurring in persons with advanced pulmonary tuberculosis, often develops so insidiously that it escapes recognition. Diffuse pneumothorax, however, usually makes its presence known by acute pain in the side, severe dyspnea, spas-

[1] Arch. of Pediatrics, 1903, xx, 817.
[2] Deut. med. Woch., Nov. 22, 1899.
[3] Wien. klin. Woch., Dec. 21, 1899.

modic cough, cyanosis and mental anxiety. In some cases there is also decided shock.

**Physical Signs.**—*Inspection* usually reveals considerable enlargement of the affected side, obliteration or even bulging of the interspaces, impaired mobility, and displacement of the heart to the opposite side. Litten's diaphragm phenomenon is absent. On *palpation* the vocal fremitus is diminished or abolished over that part of the chest which contains the air. In right-sided pneumothorax, the hand may also detect the edge of the liver some distance below the ribs.

*Percussion* usually yields a loud, hyperresonant note, often extending considerably beyond the normal lung boundaries. In some cases the note is distinctly tympanitic, but when the intrapleural tension is excessive it may be muffled or actually dull. Percussion is also useful in accurately locating the position of the neighboring organs.

*Auscultation* usually affords valuable evidence. In many cases the breath sounds and voice sounds are entirely absent. In other instances these sounds are well transmitted and have a peculiar amphoric or metallic quality. This may be the case not only in open pneumothorax with a free passage of air in and out of the cavity, but also in closed pneumothorax when the lung is solidified and atelectasis is incomplete. Metallic tinkling, a sound compared by Laennec to that which is produced by the dropping of a pin into a metallic or porcelain jar, is often present. This phenomenon has usually been attributed to the falling of a drop of liquid from a moist pleura upon the surface of accumulated fluid, but Barach[1] has shown that it is probably produced in the majority of cases by a bubble of air coming up through effusion from a fistulous opening in the lung below the level of the fluid. Possibly in some instances it is due to a râle produced in a bronchus or a pulmonary cavity close to the pneumothorax. In any case the sound acquires its peculiar metallic quality by transmission through the air-filled cavity, which acts as a resonator. Of special importance is the sign known as bell tympany (bruit d'airain of Trousseau). This sound is to be heard by applying the stethoscope over the front or back of the chest while an assistant percusses in the neighborhood or at a point directly opposite, using two silver coins, one as a plessor and the other as a pleximeter. It is a ringing, anvil-like sound, quite unlike the chink that is yielded by the healthy lung.

Additional signs are present in hydropneumothorax and pyopneumothorax when the quantity of fluid is considerable. Corresponding to the position of the liquid effusion there is a zone of dulness or flatness which is extremely movable. As the lung is prevented by the air from exerting any retractile force, the fluid obeys the law of gravitation and therefore its upper level remains horizontal in every position of the patient. In many cases if the patient be gently shaken while the ear is applied to the chest a loud splashing sound is produced (Hippocratic succussion splash). Occasionally this splash can be heard at a distance. Purulent effusion usually gives rise to symptoms of septic infection.

*X-ray.*—Fluoroscopic examination of the chest with the patient in a sitting posture reveals an area of great transparency corresponding to the site of the pneumothorax. In hydropneumothorax and pyopneumothorax there is below this area of transparency a uniform shadow which moves freely with each respiration and each change of posture. On shaking the patient even the splash may be seen.

**Diagnosis.**—As a rule pneumothorax is readily recognized. In the

[1] Archives of Diagnosis, Jan., 1910.

comparatively rare cases in which there is dulness on percussion there is some danger of mistaking the disease for a *pleural effusion*. If necessary, exploratory puncture should be employed to clear up the difficulty.

Pneumothorax is not likely to be confused with *emphysema*, as the latter develops gradually, is usually bilateral, and does not cause lateral displacement of the heart. In emphysema, too, the coin test is negative and metallic tinkling is absent.

A large *tuberculous cavity* sometimes produces signs similar to those of circumscribed pneumothorax. But a cavity is usually located near the apex of the lung; it may displace the heart toward the affected side, but never in the opposite direction; and it often yields pectoriloquy, which is rare in pneumothorax. Moreover, over a cavity the chest wall is often flattened, succussion splash is absent and the coin test, except in very rare instances, is negative.

*Diaphragmatic hernia* may simulate pneumothorax very closely. The data in favor of hernia are abdominal pain, vomiting, hiccough, and loud peristaltic gurgling sounds on auscultation. Fluoroscopic and radiographic examinations, however, are the most certain means of distinguishing between the two conditions.

Keen judgment is sometimes required in differentiating pneumothorax from *subphrenic pyopneumothorax*. Not infrequently the diagnosis is determined largely by the antecedent history. When the collection is below the diaphragm the heart is rarely displaced, vesicular breathing is often present over the greater part of the lung, and Litten's shadow is usually visible. X-ray examinations usually afford valuable aid in the diagnosis.

**Prognosis.**—The prognosis depends largely upon the condition of the patient at the time of the accident and the extent of the lesion. In tuberculous cases pneumothorax usually proves fatal. Death may occur within a few hours, but more frequently it is delayed for several weeks. In some cases the condition becomes chronic and life is prolonged for months or years. Cures are exceptional, but do occasionally occur. On the other hand, pneumothorax developing in healthy individuals as the result of traumatism or of severe muscular exertion is comparatively benign. Of 56 cases of spontaneous non-tuberculous pneumothorax collected by Fussell and Riesman[1] all but one ended in recovery.

**Treatment.**—Unless the symptoms are pronounced no active treatment is indicated. At the onset morphin may be required to relieve pain, cough and dyspnea, and diffusible stimulants to combat the condition of collapse. Severe pressure-symptoms, however, demand intervention. Enough air should be removed from the pleural cavity by thoracentesis to relieve the tension, but forcible aspiration should be avoided, as a certain degree of pressure favors closure of the pulmonary fistula. In cases of valvular pneumothorax a free opening in the chest-wall may be necessary to secure relief. In hydropneumothorax the serous effusion should not be disturbed, at least for several weeks, unless it is causing discomfort and even then only enough fluid should be removed to relieve the intrapleural tension. In tuberculous cases the replacement of the fluid by nitrogen gas has sometimes proved very satisfactory. Pneumopyothorax is, as a rule, best treated by free incision and drainage, unless the condition of the patient's lungs is too far advanced to admit of such a radical procedure.

[1] Amer. Jour. Med. Sci., Aug., 1902.

## HYDROTHORAX

Hydrothorax, or dropsy of the pleural cavity, is commonly part of a general dropsy occurring in the course of chronic kidney disease, chronic heart disease, or profound anemia. It is usually bilateral, although in chronic heart disease, especially chronic myocarditis, it is often confined to one side, as a rule the right, or if bilateral, is much greater on the right side than on the left. Various explanations have been offered for this greater frequency or preponderance of right-sided effusion in heart disease. Steele and Stengel[1] suggest that it is due to compression of the azygos vein by a dilated right auricle, while Fetterolf and Landis,[2] as the result of their investigations, conclude that it is due to compression of the pulmonary veins at the root of the lung by dilated portions of the heart, especially the right auricle. Unilateral hydrothorax may also be due to compression of the venous trunks by an aneurysm of the aorta or by a tumor of the lung or mediastinal structures.

**Morbid Anatomy.**—The fluid is watery, of low specific gravity (1005 to 1015), and poor in albumin and cellular elements. Endothelial cells, in groups of two or more, usually predominate in the sediment, but sometimes, especially in long-standing cases, lymphocytes may be in excess. In many cases the lung is also edematous, and not rarely when the condition persists for a long time a low grade pleuritis supervenes, in which event the effusion may combine the characteristics of a transudate with those of an exudate.

**Symptoms.**—The symptoms of hydrothorax are the result of compression of the lung and displacement of the heart, and consist chiefly of dyspnea, cyanosis, and acceleration of the pulse. The physical signs are similar to those of a serofibrinous pleurisy, but movable dulness on change of posture can usually be demonstrated more readily than in the latter, owing to the character of the fluid and the absence of adhesions. The diagnosis is, as a rule, easy, and yet the condition is somewhat frequently overlooked, because in some cases it is latent and in others it is masked by the symptoms of the primary disorder.

**Treatment** should be directed to the disease upon which the hydrothorax depends. Hydragogue cathartics and diuretics are sometimes useful. If the transudate persists, however, and, especially if it is causing any respiratory or circulatory embarrassment, thoracentesis should be done. Not rarely in cardiac cases digitalis proves ineffective until the tension in the chest is relieved by removal of the fluid.

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## CHYLOTHORAX

Effusions of a milky appearance in the pleural sac are uncommon. The fluid may be chylous, chyliform or pseudochylous. **True chylothorax** may result from (1) rupture of the thoracic duct or its radicles, in injuries of the chest, or from (2) obstruction of the duct by tumors, enlarged lymph-nodes, thrombosis of the left subclavian vein, or filariasis. It is usually unilateral and in about one-third of the cases is accompanied by chylous ascites. The fluid is white or pinkish-white, neutral or alkaline, and very resistant to putrefaction. It contains a small amount of fat, usually less than 1 per cent., in the form of minute globules. **Chyliform effusions** are usually associated with tuberculosis or malignant disease. The fluid resembles that of true chylothorax but the fat is derived from the degeneration of cellular

[1] Univ. of Penna. Med. Bulletin, 1901.
[2] Amer. Jour. Med. Sci., Nov., 1909.

elements. The percentage of fat is usually higher than in chylothorax, (often 3 or 4 per cent.), and the globules are larger, and are associated with many endothelial cells and leucocytes in various stages of degeneration. *Pseudochylous effusions* are also milky, but they are said to contain little or no fat. The opacity or turbidity is probably due to a compound of lecithin and globulin in suspension (Wallis and Scholberg[1]), although it has been ascribed to other causes. Pseudochylous effusions have been observed in association with cardiac disease, cirrhosis of the liver, chronic nephritis, and especially renal syphilis.

**The symptoms and physical signs of chylothorax** are those of hydrothorax or serofibrinous pleurisy. The condition is rarely suspected until the milky fluid is obtained by aspiration. The differentiation of true chylothorax from chyliform hydrothorax and pseudochylous hydrothorax is sometimes difficult. Intermediate forms are not uncommon.

**Treatment.**—Aspiration is required in chylothorax when pressure-symptoms are present, but the entire effusion should not be withdrawn, as a certain degree of pressure may be necessary to prevent the escape of more fluid from the duct. Chyliform and pseudochylous effusions should be treated as serofibrinous pleurisy or as hydrothorax, according to the nature of the underlying condition.

## HEMOTHORAX

Hemothorax is an extravasation of blood into the pleural cavity. It is to be distinguished from a hemorrhagic pleural effusion the result of pleurisy. The condition is most frequently due to a penetrating wound of the chest with rupture of an intercostal artery or an intrathoracic vessel. Less commonly it arises from the spontaneous rupture of a thoracic aneurysm or the erosion of an intrathoracic vessel by an abscess or malignant growth. Occasionly it is observed in the course of hemophilia or purpura hemorrhagica.

**Symptoms.**—Hemothorax gives rise to the symptoms and physical signs of hydrothorax and, in addition, if the extravasation is large and takes place rapidly, symptoms of severe hemorrhage, such as pallor, restlessness, sighing respiration, faintness, etc. Even if there are no conspicuous indications of internal bleeding, hemothorax may be suspected when signs of pleural effusion quickly develop after traumatism of the chest or in the course of aortic aneurysm.

The **prognosis** depends upon the cause and the severity of the hemorrhage. Even with comparatively large effusions spontaneous absorption is of frequent occurrence. In the case of penetrating wounds of the chest there is always considerable danger of infection and consequent empyema. The **treatment** is largely surgical. Small effusions without any external wound or rupture of the lung do not require operation. If pressure-symptoms become marked, the blood should be evacuated without delay, and if infection supervenes, the condition should be treated as for empyema.

[1] Quart. Jour. of Med., 1910 and 1911.

# DISEASES OF THE CIRCULATORY SYSTEM

## DISTURBANCES OF THE CARDIAC RATE AND RHYTHM

**The Pulse Rate.**—The average frequency of the pulse in the healthy adult at rest is about 72 for men and 80 for women. In new-born infants it is between 140 and 120, and in the second year it is between 110 and 120. The frequency of the pulse is temporarily increased by physical exertion, mental excitement, eating, and the use of stimulants. It must be borne in mind that the pulse-rate at the wrist does not always correspond with the heart-rate. This is due to the fact that in certain pathologic conditions some of the ventricular contractions are too weak to produce peripheral pulse waves.

**Tachycardia.**—By this term is meant increased frequency of the cardiac action. Some writers restrict the term, however, to a rate above 130 per minute. As a pathologic phenomenon tachycardia may be due to: (1) pyrexia; (2) the action of certain drugs, such as thyroid extract and belladonna; (3) hyperthyroidism; (4) various forms of cardiac disease; (5) severe anemias; (6) acute circulatory weakness from any cause, and (7) paroxysmal tachycardia.

In pyrexia the pulse and temperature curves usually run parallel, in adults the pulse-rate increasing by about eight beats for every Fahrenheit degree above the normal, although there are many exceptions to this rule. In certain diseases, such as scarlet fever and septicemia, the pulse-rate is often increased out of proportion to the elevation of temperature, and in others, such as cerebral meningitis and yellow fever, the reverse is sometimes true. During infancy the increase in the pulse-rate for each degree of temperature, other things being equal, is much less than in adults.

**Bradycardia.**—This term is sometimes restricted to infrequency of the ventricular contractions, but it is more commonly employed to denote infrequency of the pulse-rate at the wrist. In certain conditions, owing to the failure of some of the ventricular contractions to produce peripheral pulse waves, the rate of the pulse at the wrist is less than normal, while that of the ventricular contractions is normal or above normal. The difference between the heart-rate and the pulse-rate is known as the *pulse deficit.*

Bradycardia (70–50) is occasionally observed as an individual peculiarity in perfectly healthy persons. It may be physiologic also in the puerperium. Pathologic infrequency of the pulse occurs in many conditions, notably in: (1) Certain forms of organic heart disease (characteristically in lesions of the auriculoventricular bundle causing partial or complete heart-block); (2) certain toxemias—icterus, hypothyroidism, uremia, digitalis poisoning, etc.; (3) lesions at the base of the brain irritating the vagus, such as meningitis or tumor; (4) convalescence from acute febrile diseases; (5) certain painful affections, such as lead colic, biliary colic, etc.; (6) cachectic states.

**Disturbances of Rhythm.**—Various forms of irregular action of the heart have long been recognized, but until recently it was impossible to classify them or to determine their exact significance. For the great advances in the study of the cardiac irregularities that have been made in the last

few years we are largely indebted to the work of Einthoven of Holland, of Mackenzie, Keith, Lewis and Cushing of England, of His and Wenckebach of Germany and of Erlanger and Cohn of this country. The two methods which have contributed most to the subject are the use of the polygraph, which makes simultaneous tracings of the waves produced in the jugular vein by the movements of the right auricle and those produced in the radial artery by the movements of the left ventricle, and the use of the electrocardiograph, which records the movements in the string of a galvanometer produced by electric currents generated by the contractions of the cardiac muscle.

A knowledge of the conduction system of the heart and of the waves of the venous pulse is necessary for a proper understanding of the functional disturbances which result in the various forms of arhythmia.

**Conduction System.**—It has been satisfactorily established that the heart-beat is conducted over certain bands or bundles of modified muscle, which represent the remains of the primitive cardiac tube. Whether the excitation to each beat is of neurogenic or of myogenic origin is not definitely known. Normally each beat starts in a small area of specialized tissue at the junction of the superior vena cava with the right auricle, described by Keith and Flack, and known usually as the *sino-auricular node*. This node is also spoken of as the "pacemaker," because it sets the pace, as it were, for the entire heart. From the sino-auricular node the wave of excitation or impulse spreads over the auricles, causing auricular contractions, and passes on to a second node, situated in the right auricle near the mouth of the coronary sinus, described by Tawara, and known as the *auriculoventricular node* (A-V node). Here it suffers some delay owing probably to the greater resistance to conduction offered by this tissue. The delay at this point is mainly responsible for the definite interval between the auricular and the ventricular contractions. From the auriculoventricular node the impulse passes directly to the ventricles through the *auriculoventricular bundle* (bundle of His), which runs along the top of the auriculoventricular septum and near the union of the posterior and median flaps of the aortic valve divides into two branches, one to the left ventricle and the other to the right, each branch subdividing into numerous fine fibers (Purkinje fibers). If for any reason the sinus region ceases to excite impulses or the impulses fail to reach their normal destination, then the auriculoventricular node or some other part of the conducting system of modified muscular tissue may assume the function of "pacemaker," and thus the normal sinus rhythm may be replaced by various forms of irregular rhythm.

Finally, it must be borne in mind that the central nervous system controls the beat of the heart even if it does not originate it. Vagus impulses tend to diminish the rate of the heart's contractions, lessen their force and impede the passage of stimuli from the auricles to the ventricles; while sympathetic impulses tend to quicken and strengthen the contractions and to improve the conduction of stimuli through the auricles to the ventricles.

**Venous Pulse.**—By the venous pulse is usually meant the pulsation which occurs in the jugular vein (usually the right jugular vein) in the neck, just above the sterno-clavicular junction. This pulsation is transmitted from the auricle below and affords a direct means of studying what is going on in that chamber of the heart. In a tracing of the jugular pulse three main waves are seen. The first wave is due to contraction of the auricle and is known as the *a* wave. Its absence signifies that the auricle is not contracting in a normal manner. Following the *a* wave there is a slight depression which in turn is followed by a second wave, the so-called *c*, or carotid wave.

This wave is caused by closure of the tricuspid valve and the emptying of the coronary veins into the auricle. The time between the beginning of the *a* wave and the beginning of the *c* wave is called the *a–c* interval. It measures, as a rule, 0.15 to 0.20 second. A longer interval than 0.20 second suggests a delay in conduction. Following the *c* wave is a definite depression called *x*, which continues until near the end of ventricular systole, when the third wave, or *v* wave occurs. This wave, which is sometimes notched, is the ventricular wave of Mackenzie or the ventricular stagnation wave of Hering. The summit of it is synchronous with the opening of the auriculoventricular valves. Following the *v*-wave is another deep depression, *y*, which is due to emptying of the auricle. In slowly-acting hearts a fourth wave, *h* or *b* wave, may be seen between the *v* and the succeeding *a* wave. Its time relation to the preceding *v* or *c* wave is constant. It is probably due to the floating backward of the cusps of the auriculoventricular valves in mid-diastole as a result of the rush of blood from the auricles into the ventricles. When the pulse quickens the *h* or *b* wave disappears.

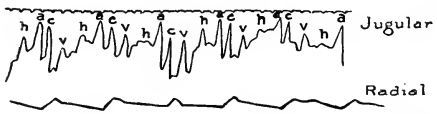


FIG. 17.—Tracings of the jugular and radial pulses showing the *h* or *b* wave.

**Forms of Cardiac Arrhythmia.**—While there are forms of cardiac arrhythmia which are difficult to classify the large majority fall into one of six groups: (1) Sinus arrhythmia; (2) extra-systole; (3) heart-block (partial or complete); (4) auricular fibrillation; (5) auricular flutter; (6) pulsus alternans; (7) paroxysmal tachycardia.

Occurring singly, most of these forms of arrhythmia can usually be recognized without the aid of instruments other than the stethoscope, but this is not always the case, and in certain forms of irregularity graphic methods by means of the polygraph or electrocardiograph are absolutely necessary for an exact diagnosis.

**The Polygraph.**—Mackenzie's ink polygraph is an instrument designed to take simultaneous tracings on the same recording surface of any two of the following: the jugular pulse, the apex-beat, an arterial pulse, and the respiratory movements. As a rule, the most satisfactory tracings for study are those of the pulse in the radial artery and those of the pulse in the jugular vein. The polygraph is of great value in the detection of many irregularities of rhythm and is particularly useful in the diagnosis of pulsus alternans.

**The Electrocardiograph.**—This instrument, which was perfected by the Dutch physiologist, Einthoven, about 1900, is designed to record the minute electric currents (1 to 3 millivolts) which the heart, like other contracting muscle, generates. With the body in a state of complete relaxation the predominant current is that produced by the movements of the heart. The instrument consists of a fine quartz or platinum thread suspended vertically in an electromagnetic field. The ends of the thread are connected by wires to the poles of the body that is to be examined. When the current from the body passes through the thread the latter is attracted to one or the other side of the magnetic field. The thread is magnified by a microscope and its shadow is projected by an arc light upon the slit of a camera in which it is photographed upon a strip of film moving at a fixed speed. Between the

instrument and the patient are several keys, the purpose of which is to bring in or throw out of circuit the body, to compensate for skin current, to calibrate the excursion of the string, etc.

The character of the electrocardiogram varies somewhat with the parts of the body from which the current is led off. Although any two parts of the body may be selected as "leads" in special cases, it is customary to use the following three, suggested by Einthoven: lead I, right arm and left arm; lead II, right arm and left leg; lead III, left arm and left leg. The normal electrocardiogram consists of upward and downward deflections, the result of auricular and

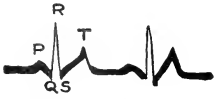


FIG. 18.—Scheme of the normal electrocardiogram.

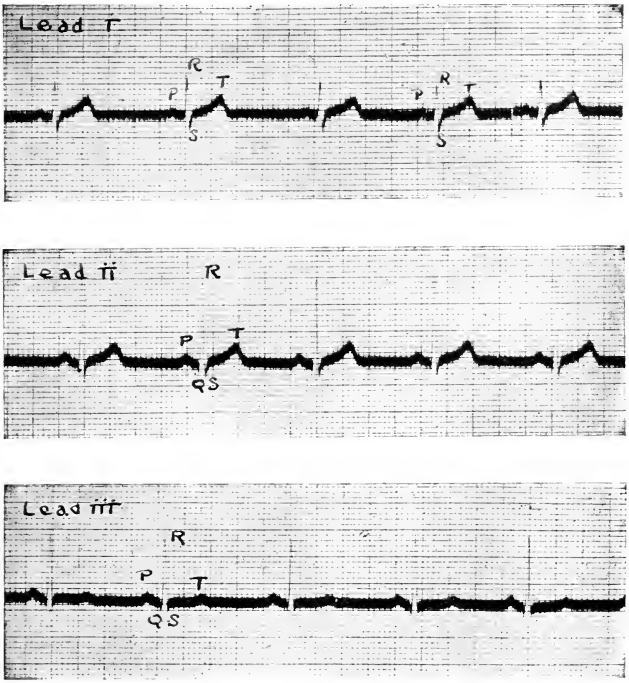


FIG. 19.—Normal Electrocardiogram.—This shows the three customary leads. The P wave is caused by electrical changes taking place in the auricles. The interval between this wave and the succeeding one is the P-R interval. This interval should be from. 12-.20 seconds. The Q.R.S. and T waves are due to ventricular activity. The amplitude of the deflection of the Q.R.S. group is greatest in lead two. Time intervals in $\frac{1}{5}$ and $\frac{1}{25}$ of a second.

ventricular activity. The first upward deflection, P, is small and due to the contraction of the auricles and the other deflections, Q, R, S, T,

are all due to the action of the ventricles. R and T are the most constant of these and so far as our present understanding goes are the most important. T is an upward deflection in lead II; it is rarely inverted in lead I, and it is not infrequently inverted in lead III. The effect of digitalis upon the heart is usually shown graphically by an inversion of the T wave in one or more leads in which it was originally upward. In patients who have not had digitalis T wave negativity in lead I is usually evidence of serious myocardial disease.

The time-distance being the commencement of auricular and ventricular contraction, and is a measure of the function of conductivity of the auriculoventricular bundle. It is shorter by one-tenth of a second than the *a–c* interval in the polygraphic tracing of the jugular pulse.

The electrocardiograph affords a means of accurate diagnosis in cardiac disease and has led to great advances in our knowledge of many obscure affections of the heart. It is not only useful in differentiating the various forms of arhythmia, but it furnishes valuable information concerning the action of cardiac remedies, and, as has been shown by Einthoven and Lewis, it definitely indicates the relative weights of the left and right ventricles. Auricular flutter cannot often be diagnosed except by the electrocardiograph. On the other hand, pulsus alternans is usually, although not invariably, better shown by the polygraph. Records can be made with the electrocardiograph in shorter time and with much less fatigue to the patient than with the polygraph, although the latter has advantages in being relatively inexpensive, and in being portable, and, therefore, available for use in the patient's home.

**Sinus Arrhythmia.**—This form of arrhythmia occurs chiefly in childhood and early adult life, although it may be observed at any age. Neurotic

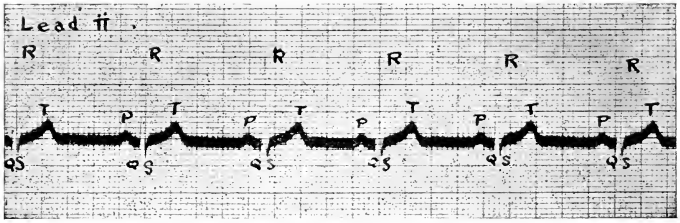


FIG. 20.—Sinus Arrhythmia. The only abnormality in this condition is a slight irregularity in the occurrence of auricular contraction—P waves—due to arrhythmic stimulus production.

individuals show a greater tendency to it than others. The irregularity is usually, but not invariably, related to phases of the respiration, being an exaggeration of the inspiratory quickening and expiratory slowing that normally occurs upon very deep breathing. The various events of each cardiac cycle are normally grouped and occupy virtually the same length of time, the characteristic feature being the varying length of the diastolic period. The irregularity is most marked when the heart-rate is slow and tends to diminish or to disappear with increased cardiac activity, the result of physical exertion or excitement. It subsides when the breath is held. It is frequently abolished also by a full dose of atropin.

Sinus arrhythmia is apparently due to an abnormal sensitiveness of the

vagi to impulses reaching the heart reflexly from various parts of the body. In many cases it is first observed during convalescence from an acute infection. It may also occur during the administration of digitalis. It has no serious significance and requires no special treatment.

**Extrasystoles or Premature Contractions.**—These constitute one of the most common forms of cardiac irregularity and are frequently productive of subjective symptoms. They are due to an abnormal irritability of the heart muscle, as a result of which stimuli for contractions arise in some part of the remains of the primitive cardiac tube besides the sinus node. The abnormal stimulus in the majority of cases emanates from the ventricle (ventricular extrasystole), less frequently it originates in the auricle (auricular extrasystole); and occasionally it arises in the vicinity of the auriculoventricular node (nodal extrasystole).

An extrasystolic beat is of smaller volume and of shorter duration than the normal beat and usually is followed by a longer pause than the average (compensatory pause), because the next impulse coming from the sinus node finds the muscle exhausted, that is, in its "refractory period," and therefore unable to respond. Premature beats may occur after each normal beat, after every second, third or fourth beat, or only at long and, perhaps, irregular intervals. Occasionally they outnumber the contractions of normal origin. With quickening of the pulse the irregularity usually diminishes or disappears. As a rule, they are abolished with a rate above 120.

Extrasystoles occur at all ages, but they are most frequent after the fortieth year, and are comparatively rare in childhood. The muscle irritability upon which they depend is usually the result of myocardial disease, but it may be of functional origin and occur in a heart that is apparently otherwise normal; thus, it may be produced by febrile diseases, by tobacco or alcohol poisoning, by overdoses of digitalis, or by various reflex disturbances.

The *ventricular extrasystole* occurs after the normal auricular systole, synchronously with it, or immediately before it. In any case it is usually followed by an abnormally long pause, the succeeding auricular impulse reaching the ventricle when it is already contracting or when it is in its "refractory" period. The next pulse beat, however, is likely to be of abnormal amplitude and strength, because the ventricle during the long pause has had extra time to fill and to recuperate. Occasionally the sinus rhythm is not disturbed, the extrasystole occurring between two normal beats (interpolated extrasystoles). If an extrasystole with its compensatory pause occurs regularly after each normal pulse-beat, a coupled rhythm, or *pulsus bigeminus*, is produced. Coupled rhythm may also result from partial heart-block. If an extrasystole with its compensatory pause occurs regularly after every two normal beats the *pulsus trigeminus* is produced. In many cases an extrasystole is so weak that it produces no pulse wave at the wrist. In this event the abnormally long pause gives rise to what is known as a "dropped beat" or *intermittent pulse*.

In *auricular extrasystoles* premature contractions begin in the auricle and usually produce premature contractions in the ventricles. In the majority of cases the *a–c* interval exceeds the normal and the compensatory pause is absent. *Nodal extrasystoles* are comparatively rare. The abnormal stimulus arises in the vicinity of the auriculo-ventricular node and passes upward to the auricle and downward to the ventricle, producing premature contraction in each chamber. These premature auricular and ventricular contractions are usually synchronous or nearly so, and in this respect differ from auricular extrasystoles in which the *a–c* interval is almost always prolonged.

Some patients are unconscious of the occurrence of extrasystoles, but

many of them experience a fluttering sensation in the region of the heart at the time of the premature contractions, or have a feeling that the heart intermits, or complain of the violent "thump" which follows the compensatory pause. Occasionally during the long pause there is a feeling of faintness, and very rarely actual syncope occurs, the condition thus simulating the Adams-Stokes syndrome due to heart-block.

Ordinarily extrasystoles can be recognized by palpation and auscultation alone. In counting the pulse it will be found that the regular sequence of beats is interrupted at certain intervals by the occurrence of an early wave

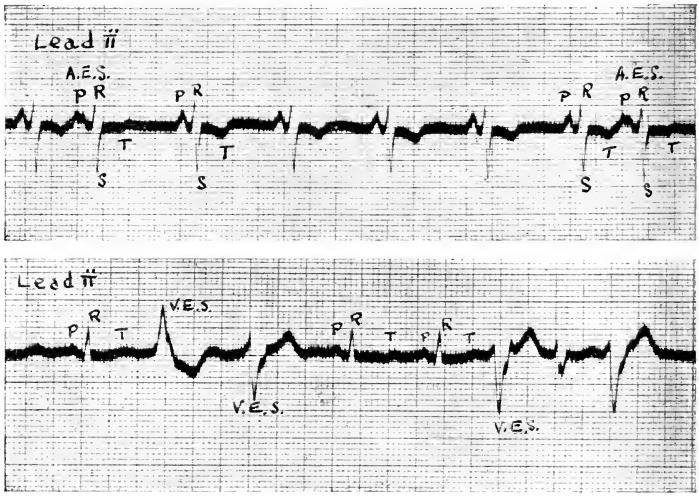


FIG. 21.—Auricular extrasystoles. In two cycles P waves are seen to occur prematurely. These waves are seen to be of different shape from the normal P waves. The former arise in some ectopic focus, hence the difference in shape. The T waves in this tracing are inverted.

FIG. 22.—Ventricular extrasystoles. Extrasystoles can be identified as arising from at least two foci in this tracing. Two such waves are seen occurring together in the third and fourth cycles of this tracing. These waves are identified by their prematurity, their size and shape, by the longer time interval they occupy, and by the absence of a preceding P wave.

which is followed by a pause of unusual length or that an otherwise regular pulse is interrupted from time to time by a pause of longer duration than the average. If there is merely an unusually long pause or intermission the condition may be mistaken for *partial heart-block*, but in extrasystole the premature beat can usually be heard or felt at the cardiac apex, whereas in heart-block there is an entire absence of ventricular contraction during the pulse intermission. Moreover, dropped beats due to heart-block usually recur more regularly than premature contractions. Extrasystoles may sometimes simulate *auricular fibrillation* but in the latter the pulse is completely irregular both as to force and time, strong beats may follow short pauses and weak beats, long pauses, and the irregularity increases with quickening of the pulse-rate. Complicated cases of extrasystolic irregularity can be

recognized with certainty only by means of polygraphic or electrocardiographic tracings.

**Heart-block.**—This form of irregularity depends upon defective conductivity of the impulse to contraction at some point in its course, usually in the bundle of His (*auriculoventricular heart-block*). The impulse in passing from the auricle to the ventricle may be merely delayed, so that the ventricular contractions do not follow the auricular contractions as soon as they should, or certain impulses may fail to reach the ventricle so that an occasional ventricular beat is "dropped," or, perhaps, every third or fourth one is regularly missed. These two degrees of impaired conductivity are described as *partial heart-block*. In other cases no impulses pass from the auricle to the ventricle and as a result the two chambers contract independently of each other, the auricle responding as usual to sinus stimuli and the ventricle initiating a rhythm of its own, which is much slower than that of the auricle. This condition is known as *complete heart-block*. The cause of the defective conduction may be functional or organic. Functional block is, as a rule, the result of the excessive use of digitalis. Organic block may be due to an acute or chronic lesion. Thus, it may occur in the course of infective diseases, such as acute rheumatism, influenza or diphtheria, as a result of acute inflammatory changes in the auriculoventricular bundle, or it may depend upon sclerotic changes in the bundle occurring as a part of a wide-spread degeneration of the cardiac muscle. Occasionally, the lesion is restricted solely to the bundle of His and consists of a gumma, tumor, or infarction. A few cases of congenital heart-block have been reported.

The only indication of a slight degree of depression of conductivity may be a lengthening of the *a–c* interval. In greater degrees of defective conductivity "dropped" beats occur. Every second, third or fourth auricular impulse may excite a ventricular contraction, producing a so-called 2:1, 3:1, or 4:1 heart-block. When each third or fourth auricular impulse fails to reach the ventricle a bigeminal or trigeminal pulse results (see p. 635). In complete heart-block the pulse is usually below 40 per minute, and often it is between 30 and 20. Occasionally, however, it is 50 or even 60 per minute. In complete heart-block the number of ventricular contractions is uninfluenced by physical exertion, mental excitement or fever, but in incomplete heart-block these factors may increase the number of dropped beats. Except in slight grades of heart-block the rhythm is usually regular, unless ventricular extrasystoles are also present. In many cases jugular pulsation may be noted on simple inspection as occurring at a much more frequent rate than that of the radial or carotid artery.

Subjective symptoms are not always present, even in complete heart-block. The latter, however, and even the severer grades of partial heart-block, by causing temporary anemia of the brain, may produce the *Adams-Stokes syndrome*, which is characterized by attacks of syncope or giddiness or by epileptiform convulsions. These phenomena are always accompanied by marked infrequency of the pulse and may occur at intervals of days, weeks, months, or years. Complete heart-block and the higher grades of partial heart-block can usually be recognized by palpation and auscultation alone. In slight depression of conductivity and in heart-block complicated by other forms of arhythmia an exact diagnosis cannot be made without the aid of the polygraph or electrocardiograph. The less severe grades of partial heart-block, occurring in the course of acute infections, are often temporary. The chronic forms of heart-block are serious. Nevertheless, if there are no accompanying indications of pronounced cardiac insufficiency the condition is not entirely incompatible with many years of fair

health. The average life expectancy in high grade heart-block is about three years. In syphilitic cases recovery has occasionally occurred under antiluetic treatment.

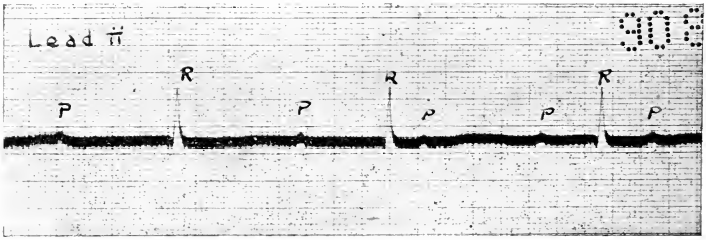


FIG. 23.—Complete heart-block. There is complete dissociation of auricular and ventricular activity. Each is beating regularly, but at different and independent rates.

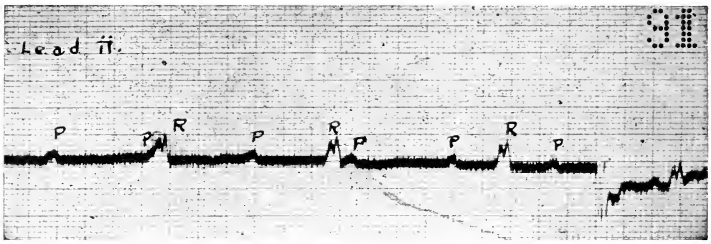


FIG. 24.—Complete heart-block. The auricular waves occur regularly, but at a faster rate and independently of the ventricular waves. The R waves in this tracing are notched due to some delay in conduction along one branch of the bundle of His.

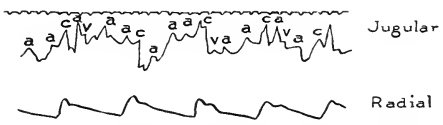


FIG. 25.—Complete auriculoventricular heart-block as shown by simultaneous tracings of the jugular and radial pulses.

*Intraventricular Block.*—Occasionally disturbance of conduction occurs after the cardiac impulse has passed the bifurcation of the auriculoventricular bundle, that is in one or both main branches of the bundle or in the arborizations of a branch. This condition, which is known as intraventricular block, can be recognized only by electrocardiography. It is frequently associated with other disturbances of cardiac function and is of serious significance, being usually indicative of advanced myodegeneration.

*Sino-auricular Block.*—This is a comparatively rare form of cardiac disturbance, of little or no pathologic significance, in which the auricular beat is lost as well as the ventricular, the rhythm of both chambers being interrupted by a cycle of unusual length. It may be suspected when the pulse is irregular as the rate returns to normal after exercise and no other evidence of circula-

tory fault is present (Smith[1]). The irregularity produces no subjective symptoms and is not influenced by respiration. It can be readily identified electrocardiographically.

The *treatment* of heart-block is that indicated by the underlying condition. Atropin tends to increase conductivity but it is without effect except in functional complete block, in which it may lessen or remove the block. In complete block digitalis has no influence on the rate of the ventricular contractions and may be given if other symptoms are present indicating its use. Partial heart-block, however, may be converted into complete heart-block by its administration.

**Auricular Fibrillation.**—In this condition the uniform contractions of the auricle as a whole are replaced by a multitude of haphazard contractions, and as a result the ventricular beats and pulse beats become extremely irregular, both as to time and to force. The condition has also been called "delirium cordis" and "pulsus irregularis perpetus."

Auricular fibrillation frequently occurs in association with chronic valvular disease, especially mitral lesions, the result of rheumatism or chorea.

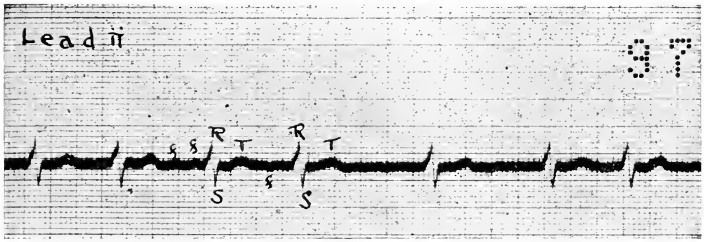


FIG. 26.—Auricular Fibrillation. P waves are absent. Fine fibrillation waves "f" can be seen. The ventricular action is completely arrhythmic as indicated by the irregular production of R waves.

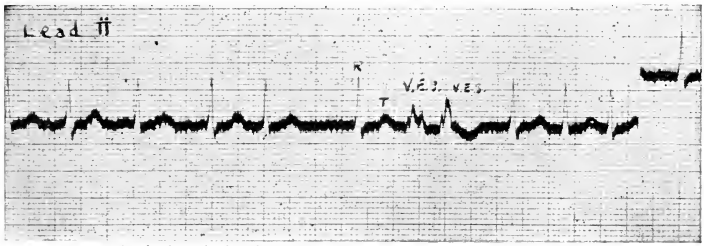


FIG. 27.—Auricular Fibrillation. There is complete irregularity of ventricular activity. There is an absence of P waves. This tracing is interrupted by two ventricular extrasystoles.

After middle life it is more often observed as an accompaniment of myocardial degeneration (chronic myocarditis). Transitory fibrillation is not rarely seen in acute infective diseases, such as rheumatism, pneumonia, diphtheria, etc., and in the course of hyperthyroidism. It sometimes results from excessive digitalization. Occasionally it occurs as a consequence of physical strain in persons who seem to be otherwise normal. *About two-thirds*

[1] Amer. Jour. Med. Sci., Oct., 1921.

*of all cases of serious cardiac failure with edema are due to or are aggravated by auricular fibrillation.*

The pulse waves are, as a rule, considerably accelerated and wholly irregular both as to time and size, although if conduction is seriously impeded they may be normal in rate and rhythm. In the majority of cases there is a pulse deficit (less beats in the radial artery than at the apex), because many of the ventricular contractions are too weak to produce pulse waves. In contrast to sinus and extrasystolic arhythmias the more rapid the pulse in fibrillation, the greater the irregularity. The jugular vein shows no pulse or only one of a positive type produced by the ventricular systole. In the phelbogram and cardiogram there is an absence of the normal auricular, or *a*, wave. In cases of mitral stenosis the rumbling presystolic murmur disappears or is replaced by a soft diastolic murmur.

Patients with auricular fibrillation frequently complain of a sense of fluttering in the region of the heart, especially on exertion. Attacks of palpitation are common, and occasionally true paroxysmal tachycardia occurs as a result of the condition. Signs of cardiac insufficiency are usually present if the pulse rate is rapid. Angina pectoris, however is rare. Auricular fibrillation can be recognized usually by palpation of the radial pulse and auscultation of the heart, and always with certainty by polygraphic or electrocardiographic examinations.

Occurring in the course of chronic valvular and myocardial disease, auricular fibrillation is usually permanent. In some cases, however, it disappears. Recovery has not rarely been observed after removal of focal infection or the performance of thyroidectomy for hyperthyroidism. Generally speaking, it is of grave omen, nevertheless some patients who are able to lead quiet lives live for a number of years. The prognosis is, as a rule, better when the pulse can be kept approximately within normal limits by rest and medication. Digitalis is the most useful remedy. Its inhibitory effect on conductivity serves to prevent many of the excessively numerous contractions of the auricle from reaching the ventricle and exhausting it. In the absence of untoward effects the drug should be given until the pulse falls to about 70, when it should be stopped for several days, and then resumed in smaller doses. In the majority of cases it is necessary for the patient to continue the digitalis for the remainder of his life. Quinidin may abolish auricular fibrillation by depressing irritability and conductivity in the auricular muscle (see p. 653). It succeeds in from 40 to 50 per cent of the cases, although relapse usually occurs in from a few days to several months. Patients with auricular fibrillation as a result of exophthalmic goiter or of thyrotoxic adenoma may be definitely improved by surgical treatment of the primary condition.

**Auricular Flutter.**—In this condition the auricular contractions are extremely rapid (180 to 400 per minute), rhythmic and of uniform amplitude. The impulses, instead of being generated incoördinately in many foci in the auricular wall, as in fibrillation of the auricle, arise from a single focus outside of the normal pacemaker. The rate and rhythm of the ventricular contractions depend largely upon the functional activity of the auriculoventricular bundle. In many cases there is partial heart-block, the ventricle contracting one-half as frequently as the auricle and regularly. However, with complete heart-block there may be bradycardia and with inconstant degrees of conductivity there may be marked irregularity. Exertion may change somewhat the rate and even the rhythm of the ventricular contractions, but there is no gradual decrease of the rate after exercise, such as occurs with the normal heart.

The etiology of auricular flutter is apparently much the same as that of

auricular fibrillation; indeed, the two conditions may occur in the same patient at different times. Flutter may be paroxysmal lasting a few hours or days, but, as a rule, it continues for much longer periods. It is almost always indicative of myocardial insufficiency and, on the whole, is of serious significance, but it does not necessarily imply an early demise, and in some instances it disappears upon the removal of some extracardiac condition, such as hyperthyroidism or focal infection. F. M. Smith[1] reports 2 cases in which paroxysms extended over 5 and 9 years respectively, and Lewis cites an instance in which flutter persisted for 6 years.

There is a close resemblance between auricular flutter and paroxysmal tachycardia, and an exact diagnosis is frequently impossible without the use of the polygraph or electrocardiograph. When the ventricular contractions are irregular the condition may simulate *auricular fibrillation*, but in the latter the arterial curves are wholly irregular while in the former groups of beats of equal

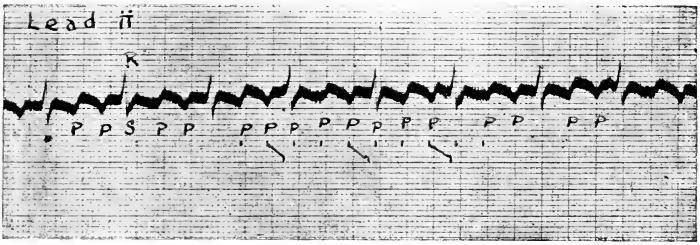


FIG. 28.—Auricular Flutter. The auricular waves occur perfectly regularly. The auricular rate is 288. The ventricular rate is 96. There are therefore three auricular contractions to one ventricular beat.

length constantly recur and bear a definite relationship to each other. In the electrocardiogram, even though the ventricular contractions are extremely irregular, the oscillations are rhythmic and constant in form for each lead, and the R deflections occur at regular intervals and do not vary in amplitude from cycle to cycle. In complete heart-block neither flutter nor fibrillation can be recognized without the aid of graphic studies. The treatment of auricular flutter consists in absolute mental and physical rest and the use of digitalis in large doses. Digitalis not rarely transforms auricular flutter into auricular fibrillation. As previously stated, the removal of focal infection or of hyperthyroidism sometimes produces marked improvement or even apparent recovery.

**Pulsus Alternans.**—This is a condition of the pulse in which strong and weak beats alternate, but in which the cardiac rhythm is normal (White). It is probably due to depressed contractility of the ventricle, and, occurring apart from auricular flutter and paroxysmal tachycardia, it signifies a badly damaged myocardium. White[2] found a mortality of 94 per cent. within 3 years in patients presenting the higher grades of pulsus alternans. The condition is found most often in elderly persons, and in association with enlargement of the heart and signs of myocardial insufficiency.

Pulsus alternans can often be detected by palpation of the radial artery or by auscultatory method of blood pressure estimation, the pulse rate being

[1] Amer. Jour. Med. Sci., July, 1921.
[2] Amer. Jour. Med. Sci., Jan., 1919.

halved at a pressure just below the systolic reading if alternation is present. A polygraphic or electrocardiographic tracing puts the diagnosis beyond doubt. As a rule, the polygraphic tracing is more dependable than electrocardiogram. The condition must be distinguished from pseudoalternation due to a rapid respiratory rate or to a pulsus bigeminus caused by late premature (extrasystolic) beats alternating with beats of normal origin. Pseudoalternation resulting from respiratory influences may be excluded by having the patient hold his breath for a few seconds. Pseudoalternation due to premature contractions cannot be excluded definitely without graphic records. The treatment of pulsus alternans is that of the underlying myocardial condition. Complete rest, both mental and physical, is always indicated.

**Paroxysmal Tachycardia.**—This term is applied to a comparatively rare condition in which there are attacks of excessively rapid heart action, with an abrupt onset and an equally abrupt termination. The rate of the the pulse is seldom less than 160 and it may be as high as 300. Usually the patient complains of palpitation and a sense of constriction or pressure in region of the heart. Occasionally there is also a feeling of "air hunger," and if the paroxysm is a long one it may be attended by general weakness and signs of circulatory failure. Between the attacks the patient is usually in good health. The seizures vary in duration from a few minutes to several days. They may occur spontaneously or they may be precipitated by excitement, straining at stool, flatulence, or even a sudden change of posture, and not rarely they are arrested by deep breathing, belching, vomiting, or even forcible efforts at swallowing. The paroxysms may be separated by intervals of weeks, months or years, or several of short duration may occur in a single day. If they are transitory, infrequent, and unaccompanied by evidences of cardiac insufficiency the outlook is usually good, at least so far as the risk to life is concerned. On the other hand, if they are of long duration, and of frequent occurrence, and are attended by obvious signs of circulatory failure the prognosis is correspondingly unfavorable. Death during an attack is comparatively rare. The condition may usually be distinguished from *simple tachycardia with sinus rhythm*, the result of infection, psychic disturbances, etc., by the absence of obvious cause and by the abrupt onset and termination of the seizures. Paroxysmal tachycardia resembles auricular flutter, but the two phenomena are apparently distinct. In paroxysmal tachycardia, as contrasted with *auricular flutter*, there is often no evidence of myocardial disease; the symptoms occur in comparatively brief attacks, frequently over a period of many years; the rate of the cardiac contractions during an attack is not usually influenced by digitalis, by exertion or emotion, or by vagal stimulation, but vagal stimulation often brings about the cessation of a paroxysm. An exact diagnosis can be made readily by means of the electrocardiograph.

The *treatment* of paroxysmal tachycardia is unsatisfactory. Some patients can arrest the paroxysms by taking deep breaths, by holding the breath, by swallowing large objects, or by vomiting, and occasionally firm pressure over the vagus brings relief. Digitalis usually fails, but the intravenous injection of strophanthin has occasionally been of benefit in prolonged attacks. This drug should not be used, however, if the patient has been taking digitalis by the mouth within a week. An ice-bag or a sinapism over the heart is sometimes of service.

## ACUTE MYOCARDITIS

**Definition.**—Although the term acute myocarditis really means acute inflammation of the heart muscle, it is commonly employed in a broader sense to designate the changes in the myocardium brought about by acute infectious processes, even though these changes may be of a degenerative rather than of an inflammatory nature. Simple and suppurative forms of the disease are recognized. The latter are comparatively rare.

**Etiology.**—Acute simple myocarditis is invariably the result of some acute infectious disease, such as acute rheumatism, chorea, diphtheria, influenza, septicemia and syphilis. In children it is most frequently of rheumatic origin. In diphtheria it is the chief cause of death. It is more common in the early stages of syphilis than is generally supposed. The myocardium may be the only part of the heart affected, but in many instances endocarditis or pericarditis is also present. Indeed, in rheumatism it is exceptional to find myocarditis unaccompanied by endocarditis or pericarditis. Not rarely all three parts of the heart are involved simultaneously, the condition being really one of carditis or pancarditis.

Acute suppurative myocarditis is chiefly met with in the course of general pyemic diseases, especially ulcerative endocarditis, the heart muscle becoming involved through the entrance of septic emboli into the coronary arteries or, less frequently, through the direct extension of a septic endocarditis or pericarditis.

**Morbid Anatomy.**—The changes may be so slight as to escape detection with the unaided eye. In well-marked cases the heart is pale, soft and flabby. The cavities are sometimes dilated. Microscopically, the lesions are found to be most pronounced, as a rule, in the tissue about the left auriculoventricular ring and in the papillary muscles of the left ventricle (Krehl). The fibers are swollen; the protoplasm is filled with fine dust-like granules which resist the solvent action of ether, but disappear on the addition of acetic acid (cloudy swelling); and the nuclei are obscured and often distended or divided. When the process is advanced fatty or hyaline changes in the muscle are also present. Occasionally, the fibers show segmentation, but this probably is an agonal lesion. In cases of true myocarditis the interstitial tissue, especially about the blood-vessels, is infiltrated with round cells, either singly or in groups. The capillaries are overdistended and small extravasations of blood are not infrequently noted. Here and there the arterioles may be blocked by hyaline thrombi. Degenerative changes have also been observed in the ganglion cells. In rheumatic myocarditis the so-called bodies of Aschoff[1] are an almost constant finding. These bodies consist of focal collections of large pale wandering cells with large vesicular nuclei. They are usually periarterial and are to be seen chiefly in the posterior wall of the left ventricle near its base.

In suppurative myocarditis there may be a large solitary collection of pus, or a vast number of purulent foci, varying in size from a pin's head to a pea.

**Symptoms.**—The symptoms are variable and are often masked by those of the primary affection. Mild forms may be manifested only by changes in the pulse and heart sounds. The pulse is feeble and usually, but not invariably, increased in frequency. It is especially sensitive to exertion. In some cases there is arhythmia due to extrasystoles or to auricular fibrillation, and occasionally there is bradycardia, due to irritation of the vagus or to heart-block. The heart-sounds, with the exception of the second pulmonic, which is sometimes accentuated, are weak and short. Not rarely the first or second

[1] Verh. d. Deut. Path. Gesellsch., 1904, viii, 46.

is reduplicated, and if the heart's action is very rapid gallop rhythm may be present. In a large proportion of cases a soft systolic murmur is audible over the mitral or tricuspid area as a result of muscular (relative) mitral or tricuspid insufficiency. The blood pressure is usually low. Severe types of the disease are characterized by great restlessness and weakness, pallor, epigastric pain, vomiting, syncopal attacks, and signs of acute dilatation of the heart. Dyspnea is not usually a conspicuous feature and cyanosis and edema are by no means common. Pain of an anginoid character is occasionally present. In some cases, especially of those occurring during convalescence from diphtheria, the condition remains entirely latent until a sudden, and perhaps fatal, attack of syncope occurs.

The symptoms of suppurative myocarditis are similar to those of acute ulcerative endocarditis (see p. 672).

**Diagnosis.**—The diagnosis is sometimes difficult. In any acute infection acute myocarditis should be suspected if symptoms of cardiac weakness develop rapidly and are out of proportion to the severity of the primary disease. Weakness of the heart sounds with instability of the pulse, precordial distress, pallor, vomiting, a tendency to syncope, and an increase in the area of cardiac dulness are especially significant. It must be borne in mind that in diphtheric and influenzal myocarditis the symptoms may not appear until some time after those of the primary disease have disappeared.

**Prognosis.**—The outlook varies with the severity and location of the lesions. The most serious cases of simple myocarditis usually occur in rheumatism or diphtheria. Marked pallor, vomiting, syncopal attacks, and a greatly accelerated pulse or marked bradycardia are symptoms of grave significance. Death may be sudden or gradual. Although mild attacks frequently end in complete recovery, it is important to bear in mind that the disappearance of the symptoms, while it removes all immediate danger, gives no absolute assurance that the heart muscle has escaped permanent injury. Indeed, there is good reason to believe that the cellular infiltration of the interstitial tissue not rarely becomes the foundation of a subsequent sclerotic myocarditis. Certainly not a few patients after the lapse of several years present signs of cardiac enlargement with mitral insufficiency.

Suppurative myocarditis is almost invariably fatal.

**Treatment.**—The indications are to arrest the inflammatory or degenerative process in the heart and to secure complete resolution, or if this is impossible, to favor the establishment of the highest degree of compensation attainable. The treatment consists largely of the measures that are called for by the causal condition and absolute rest in bed. The patient should be kept at rest for several weeks after all symptoms of the primary infection have disappeared or until the rate and rhythm of the pulse are normal. Mental and emotional excitement must also be avoided. Even after the patient is permitted to be up and about his exertions should be restricted for a long period. The diet should be light and easily digestible, with the amount of fluids somewhat reduced. The bowels should be normally moved each day. In the early stages an ice-bag over the region of the heart often serves to allay palpitation and other local discomforts, but when there is much pain a sinapism or hot poultice may be more effective. Morphin is sometimes invaluable in controlling restlessness and procuring sleep. Digitalis may be of service, but in many cases, it is useless or actually harmful. It must always be used tentatively. Attacks of acute heart failure are to be met with diffusible stimulants, such as aromatic spirit of ammonia, whiskey or camphor. Caffein subcutaneously is sometimes helpful. Strychnin also may be useful. Adrenalin, in saline solution intravenously, has been recom-

mended, but it should be used with great care lest through a sudden vasoconstricting effect it precipitate heart-failure and pulmonary edema. During convalescence, tonics, especially iron, nux vomica and quinin, may be used with advantage.

## CHRONIC MYOCARDITIS

The term chronic myocarditis is employed clinically to designate not merely a chronic inflammatory condition of the heart muscle, but also various changes of a degenerative nature in the myocardium which result in impairment of the cardiac efficiency. Unfortunately, it is not always possible to correlate the functional disability of the heart that is observed during life with the post-mortem findings. While in many cases an overgrowth of fibrous tissue or fatty change in the myocardium is clearly responsible for cardiac failure, it must be admitted that a pronounced degree of fibrous overgrowth or of fatty accumulation is often found in the bodies of persons in whom no cardiac insufficiency had been apparent or suspected, and, on the other hand, that poorly functioning hearts are sometimes observed which at autopsy show little that is pathologic either in the myocardium or valves. The explanation of these discrepancies probably rests in many instances upon the location of the lesions. An extensive lesion in the unspecialized tissue of the heart may entail much less serious consequences than a very small lesion in the highly specialized tissue constituting the cardiac conduction path. The studies of Krehl, Albrecht, Aschoff and Tawara, and others have made it clear that areas of fibrosis so minute as readily to escape detection may in certain situations, as for instance, one of the branches of the bundle of His, bring about very marked disturbances in the function of the heart.

**Etiology.**—Chronic myocardial disease is extremely common. It may occur at any period of life, but it is observed with greatest frequency after the age of 40 years. In a fairly large proportion of cases it is secondary to sclerosis of the coronary arteries. As a result of the defective circulation through these vessels a certain number of muscular fibers atrophy and degenerate, and finally may be replaced by fibrous tissue. If thrombotic or embolic occlusion of one of the coronary vessels occurs and does not prove immediately fatal, the resulting area of anemic necrosis is gradually replaced by a callous patch of fibrous tissue. In some instances syphilis, gout, and other causes of arteriosclerosis attack the myocardium directly, even before they produce any decided changes in the coronary arteries. Chronic myocarditis is not rarely a sequel of acute myocarditis, the result of rheumatism, diphtheria, septicemia, typhoid fever or some other acute infectious disease. Many of the cases with associated endocarditis or pericarditis have this origin. Chronic focal infection with its site in the gall-bladder, tonsils or elsewhere is a common cause of functional disturbances of the heart and if long continued may result in organic myocardial disease. This is true also of hyperthyroidism, which if unchecked may cause irreparable damage to the heart by charging the blood with thyroxin, the toxic constituent of the thyroid gland. Attention has frequently been called to the association of fibro-myoma of the uterus with degeneration of the heart muscle (Strassman and Lehmann, Fleck, Winter, Boldt, Baldy[1]), but the relation of the former to the latter is not definitely known. The retention of toxic substances in the blood in chronic nephritis is also a responsible factor in the production of the

[1] Amer. Jour. of Obstet., 1905, lii, 370.

disease. In mitral lesions, after a protracted period of imperfect compensation, the heart may show diffuse sclerosis with dilatation of the coronary veins and degeneration of the muscle fibers. Occasionally, fatty infiltration of the heart, probably through the pressure of the fat, is followed by actual degeneration of the cardiac muscle. Among other causes of myocardial insufficiency are diabetes, leukemia, scurvy, severe anemias, and other diseases which profoundly affect the general nutrition. Finally, in some cases of chronic myocarditis, especially of those occurring in association with high arterial tension, the primary etiologic factor cannot be determined with certainty. The disorder responsible for the hypertension, whatever it may be, may also affect adversely the nutrition of the myocardium and doubtless the hypertension itself by increasing cardiac stress may eventually cause degenerative changes in the myocardium.

**Morbid Anatomy.**—The most common lesions in chronic myocarditis are fibrosis, fatty degeneration and brown atrophy.

*Fibrosis* (*Chronic Interstitial Myocarditis, Cardiosclerosis*).—In some cases the changes are inconspicuous and may be overlooked unless the heart wall is examined in serial sections. Frequently, however, the sclerotic tissue is readily recognized and appears either as grayish streaks between the muscle-fibers or as circumscribed white patches of a tough leathery consistence. The favorite locations are the anterior wall of the left ventricle near the apex, the septum and the tips of the papillary muscles. Microscopic examination reveals an excess of connective tissue in the form of wavy bands running parallel with the muscle-fibers. The latter are often more or less atrophied and the seat of fatty or hyaline changes. When the process is well developed it is usual to find cicatricial areas wholly devoid of muscular tissue. In myocarditis due to sclerosis of the coronary arteries the tissue immediately around the affected vessels may be almost normal, while parts more remote show extensive fibroid transformation.

*Fatty Degeneration.*—This process may be diffuse or circumscribed. Even when the cause is a general one, as a cachexia or an intoxication, the left ventricle is usually the part most affected. The heart may be of normal, size, though naturally the tendency is toward dilatation. When the degeneration is slight in degree the gross appearance of the organ is almost normal, but when it is pronounced the heart-muscle is of a pale yellowish hue throughout, or, more frequently, mottled, yellowish and reddish areas alternating ("tiger heart"). The affected tissue is soft and flabby, and on section greasy to the touch. Microscopically, the fibers are found to contain minute globules of fat which are arranged in rows extending from the poles of the nucleus or are, perhaps, so numerous as to obscure both the nucleus and the striation.

*Brown Atrophy.*—This condition is found chiefly in advanced age or as a part of a general marasmus from various causes. The heart is smaller than normal, the coronary arteries are tortuous, and the muscle is flabby and often of a brownish color. Microscopically, the muscle-fibers are found to be small and to contain an excess of pigment. The latter is in the form of brownish granules (lipochrome pigments), which are grouped about the nucleus or are more uniformly distributed through the whole fiber. Many of the fibers also show fatty changes.

**Pathologic Associations and Effects.**—Chronic myocarditis is frequently associated with hypertrophy of the heart, valvular disease and general arteriosclerosis. The *cardiac hypertrophy* may be a result of the same cause which brought about the myocarditis, for instance, arteriosclerosis; it may be due to concomitant valvular disease; or it may be an effect of the myocar-

ditis itself, the undamaged muscle-fibers enlarging to compensate for those that are degenerated or destroyed. *Valvular disease* occurring with chronic myocarditis may have developed simultaneously with the latter and in consequence of the same cause, or it may be secondary to the myocardial changes, relative mitral or tricuspid insufficiency often ensuing as the result of a loss of tonicity in the myocardium and such distention of the left or right auriculoventricular ring that the normal valve leaflets are unable to close the orifice. In some instances primary endocardial lesions, by producing venous stasis in the heart muscle, give rise to a sclerotic process which has its starting point in the vicinity of the dilated coronary veins. When *general arteriosclerosis* and chronic myocardial disease co-exist, the latter is usually the secondary process, although in some cases the two conditions are produced independently through the action of the same irritant.

*Chronic nephritis* is also frequently observed in association with chronic myocardial disease, especially cardiosclerosis. This pathologic complex is known as cardiorenal disease or, if the bloodvessels also are implicated, which is usually the case, as cardiovascular–renal disease. The heart, bloodvessels, and kidneys may each be involved independently as an effect of some primary condition, such as gout or syphilis, or the disease may have its starting point in any one of the three lesions, the other two in turn developing as sequels.

For a time in chronic myocarditis, hypertrophy of certain muscular elements may compensate for functional weakness in others, but with increasing structural changes the tendency is toward *dilatation of the heart*, an accumulation of blood in its chambers and overdistention of the pulmonary and systemic veins. The effects of this general venous stasis are widespread. An important early effect is *edema*, which, as a rule, begins in the subcutaneous tissues in the dependent portions of the body. A later effect is *cyanotic induration of the organs*, especially of the lungs, liver, spleen and kidneys. This condition is characterized by atrophy and degeneration of the parenchymatous cells, excessive pigmentation, and hyperplasia of the interstitial connective tissue. It is due to the pressure of the distended veins upon the cells and interference with the nutritive exchange. In the heart the increasing pressure of the blood in the coronary veins still further impairs the nutrition of the myocardium and thus a characteristic vicious circle is established.

Occasionally a thin fibrous scar at the site of a healed infarct in the myocardium bulges outward to form an *aneurysm of the heart*. A still more rare event in cases of softened or degenerated myocardium is *spontaneous rupture* of the heart. Finally, chronic myocardial disease favors the formation of *intracardiac thrombi*. The latter are most frequently found in the auricular appendages or in the muscular interlacement near the apex. Quite frequently portions of these thrombi are carried into the blood stream and lodge in small arteries of the lungs, spleen, kidneys or other organs, causing *infarctions*.

**Symptoms.**—Occasionally chronic myocardial disease manifests itself very suddenly. Thus, a man in the prime of life, and apparently in good health, after some slight exertion, may fall in a syncopal attack and expire almost immediately. Sometimes the condition becomes at once apparent after violent or protracted muscular exercise, an acute illness, a mental shock, and injury, or a surgical operation. In the majority of cases, however, the symptoms develop insidiously, and almost invariably the first evidence, although it may be ignored for a time, is subjective. *Breathlessness on exertion* is one of the earliest manifestations. The patient perceives that

he does not breath so freely as formerly when he hurries his steps, climb, stairs, or walks against the wind. At first the dyspnea rapidly subsides, with rest, but as time goes on it does not yield so readily and it returns with less and less exertion. A sense of breathlessness sometimes occurs from psychic influences alone, but this, as contrasted with true dyspnea, is relieved by physical effort. Not infrequently cardiac dyspnea comes on also at nights just as the patient is falling off to sleep, and in some instances, when the cardiac insufficiency is more pronounced, the nocturnal attacks assume the form of so-called *cardiac asthma*. This condition, which is probably a form of pulmonary edema (see p. 605), is characterized by paroxysms of breathlessness with coughing and expectoration of thin, foamy, often blood-stained mucus.

With increasing myocardial incapacity the dyspnea becomes more marked and eventually the patient may be unable to lie down (orthopnea). Late in the disease hydrothorax, pulmonary edema, ascites, enlargement of the liver, and, perhaps, acidosis from renal insufficiency may add considerably to the respiratory difficulty. In the last stages of myocarditis, even when there has been no evidence of pronounced venous stasis, *Cheyne-Stokes breathing* may occur. In this phenomenon, which was first described by Cheyne in 1818 and again by Stokes in 1854, the respirations, at first shallow and infrequent, gradually become deeper and more frequent until a climax is reached, and then gradually wane until they cease entirely. After a period of apnea lasting from 5 to 30 seconds or even longer, the respirations recur and follow the same wave-like course. If the pause in the breathing is long and the patient is awake at the time he may lose consciousness. Contraction of the pupils and muscular twitchings may also occur during the period of apnea. Cheyne-Stokes breathing is usually an indication that death is close at hand, but it may be only transitory and occasionally it persists for months.

In a large proportion of cases sensory disturbances are the first evidence of cardiac incompetence. The character of the subjective sensation varies. There may be merely some form of *paresthesia*, or there may be *actual pain*, constant and dull, or paroxysmal and sharp and with some or all of the features of *angina pectoris* (see p. 661). It is characteristic of cardiac pain that it is brought on or aggravated by exertion and is experienced at the peripheral endings of the spinal nerves which are centrally in close relation with the afferent nerves of the heart. It may be entirely precordial, although frequently it is referred to the upper part of the chest, to the epigastrium, to the neck, to the shoulders, to the arms, or even to the wrists. Accompanying the pain or occurring independently of it, there may be other forms of cardiac discomfort, such as *palpitation* or a *feeling of fluttering* or *throbbing* within the chest. While these phenomena are not unusual apart from organic disease, their occurrence without obvious cause always calls for a thorough examination of the heart.

*Symptoms referable to the digestive organs* are common and sometimes appear before there are any other evidences of failing circulation. Fulness and oppression after eating, flatulence with noisy belching, irregular action of the bowels and enlargement of the liver may occur, and later there may be also nausea and vomiting. When these symptoms dominate the picture they are often erroneously ascribed to some primary affection of the stomach.

*Cerebral symptoms*, due to anemia of the brain, are frequently present, especially in elderly persons. Faintness, dizziness, headache, ready mental fatigue, irritability, and insomnia or sleep with disturbing dreams may all occur, and not rarely in the final stages mild delirium also appears. Occasionally, a true psychosis develops, either as a direct result of disturbance of

the cerebral circulation or as a consequence of some concomitant condition, such as renal insufficiency or excessive digitalization. Temporary interruption of the blood-supply of the brain, resulting from heart-block or very rarely from other causes is sometimes signalized by the *Adams-Stokes syndrome*, which is characterized by syncopal or epileptiform seizures in association with marked bradycardia.

A gradual *loss of flesh* with *increasing weakness* and *pallor* is not uncommon, and occurring after middle life without obvious cause should always arouse suspicion of cardiac insufficiency. General malnutrition, however, is by no means a constant feature, many patients being overweight or actually obese.

General venous engorgement, the result of dilatation of the heart and relative insufficiency of the auriculoventricular valves, occurs later in uncomplicated chronic myocarditis, as a rule, than in decompensated valvular lesions, and in many cases appears only upon the approach of the final stages of the disease. Cyanosis and edema are important indications of venous stasis. The *cyanosis* is usually confined to the lips, ears, cheeks and finger-tips. The *edema* begins, as a rule, in the dependent parts of the body and spreads upward. For a time it is often transitory, appearing during the day, if the patient is up and about, and disappearing when he is at rest in bed. Not rarely, even in severe cases, it is confined to the legs, but it may become more or less general, and sometimes it involves the serous cavities without affecting the subcutaneous tissues. *Hydrothorax* is especially common, and is found much more frequently on the right side than the left. Even when the effusion is bilateral, it is usually greater on the right side (see p. 628).

Increased engorgement of the lungs is manifested by greater dyspnea, cough, mucoid or mucopurulent expectoration, and, perhaps, signs of edema in the dependent lobes. The sputum often contains phagocytic epithelial cells loaded with granules of brown pigment (heart-failure cells). *Pulmonary infarction* is of frequent occurrence in the last stages and is usually announced by pleuritic pain and spitting of blood. With the failure of the right ventricle the *liver becomes enlarged* and tender to touch. In some cases the enlargement is extreme, the lower border of the organ extending below the level of the umbilicus. Spontaneous pain and jaundice may also occur, the last being always of grave significance. As a result of *venous stasis in the kidneys* the urine becomes scanty, and contains an excess of urates, a trace of albumin and often tube-casts and erythrocytes.

**Physical Signs.**—The physical signs are variable, but they are often few and poorly developed in comparison with severity of the symptoms. If the auriculoventricular bundle is intact large areas of the cardiac wall may be degenerate without causing any very definite signs.

*Inspection.*—The apex-beat may be in its normal position, but often it is displaced outward and downward. The impulse is usually diffused and more frequently it is weak than forcible.

*Palpation.*—In many cases the impulse seems much less forcible to the hand than it does to the eye. The radial pulse may be of normal rate, increased in frequency, or abnormally slow. Irregularity appears sooner or later in a large proportion of cases and indicates a disturbance in the conduction mechanism. Any form of arhythmia may occur, but that due to extrasystoles or to auricular fibrillation is most common. Heart-block, partial or complete, is not infrequent.

The blood-pressure also varies. In about one-half of the cases it is higher than normal. In fatty degeneration of the heart it is often low. The wall of the radial artery is usually more or less thickened.

*Percussion.*—The area of cardiac dulness may be normal, but in the majority of cases it is increased, the enlargement being more frequently to the left than to the right. In some cases, however, it seems to be proportionately enlarged in all directions.

*Auscultation.*—The cardiac sounds are not characteristic. In some cases they are simply feeble. More frequently the first sound at the apex is prolonged and muffled, or, if the disease is more advanced, replaced by a systolic murmur, due to relative mitral insufficiency. There is nothing in the quality or intensity of this murmur to distinguish it from one due to organic mitral disease. In the absence of any concomitant aortic valve lesion, the aortic second sound may be normal, although usually it is somewhat accentuated, and sometimes the second sound at the base is reduplicated. In severe cases there may be a distinct gallop rhythm.

*Electrocardiography.*—The electrocardiogram may be normal, but much more frequently it shows a preponderance of one or the other side of the heart and evidences of some disturbance of the conduction mechanism, such as extrasystoles, auricular fibrillation, auricular flutter, or heart-block. Pulsus alternans may also be indicated, but, as a rule, this is shown more clearly in the polygraphic tracing.

**Diagnosis.**—While the diagnosis of chronic myocardial disease is often easy, it is sometimes extremely difficult. Breathlessness, a sense of exhaustion, palpitation and cardiac pain occurring prematurely under effort, unless there is some other obvious cause to which they can be assigned, are always significant, and in association with enlargement of the heart, an irregularity, a murmur, or thickening of the peripheral arteries, are virtually pathognomonic. The degree of cardiac incompetence in any case of myocarditis is best determined by comparing with the individual's normal standard the amount of effort he can put forth without experiencing symptoms of cardiac distress. In applying this test due allowance should be made, of course, for any extrinsic factor that may also be affecting the heart adversely, such as anemia, overwork, loss of sleep, mental strain, etc. A number of instrumental methods have also been devised for measuring the heart's efficiency, but most of them are fallacious and few of them admit of practical application at the bedside.

The following classification of cases of chronic myocarditis suggested by the New York Association of Cardiac Clinics is simple and practical:

1. Able to carry on the patient's usual activities.
2. Able to carry on slightly to moderately curtailed activity.
3. Able to carry on only greatly diminished activity.
4. Unable to carry on any activity (without distress).

**Prognosis.**—The future of the patient with chronic myocardial disease is often difficult to forecast. Important points to be considered are the age of the patient; his social circumstances and habits; the cause of the disease and whether it is one that is likely to recur; the nature of the process, especially whether it is a stationary or progressive one; the extent and location of the myocardial lesions, so far as these can be ascertained, and the effect that the changes have already had upon the functional efficiency of the heart; the presence or absence of organic valvular disease and of complications outside of the heart, such as nephritis, hyperpiesis, arteriosclerosis, etc.; and the measure of response to appropriate treatment. In the progressive type of myocardial disease occurring after middle life the outlook is serious in proportion to the readiness with which symptoms of cardiac distress arise under effort. So-called cardiac asthma, angina pectoris, syncopal attacks, pronounced edema, and pulsus alternans are especially unfavorable indications.

The fatal issue may be the result of sudden or of gradual heart failure. Sudden death is most likely to occur in fatty degeneration of the heart, angina pectoris, and aortic regurgitation.

**Treatment.**—In the early stages of the disease treatment addressed to the causative condition not rarely serves to retard the progress of the myocardial deterioration. If there is definite evidence of syphilis antiluetic treatment is indicated; if a local focus of infection can be incriminated it should be removed, if possible; if hyperthyroidism is the causal factor thyroidectomy should be performed, unless the cardiac insufficiency is already too pronounced to justify the risk of operation; and if nephritis or hyperpiesis is the primary affection appropriate hygienic and dietetic measures are required. In many cases thorough investigation will reveal certain extrinsic factors which are contributing, more or less, to the cardiac embarrassment, such as tobacco poisoning, worry, insomnia, anemia, flatulent indigestion, etc. These, of course, should be removed if possible.

Rest and diet are important elements of the treatment. It is not always necessary that the patient should give up his occupation, but it is essential that the sum of his daily exertions should be adjusted to the working capacity of his heart. It must be borne in mind, too, that the fret and worry incident to many pursuits may exert as baneful an effect upon the circulation as undue physical effort. In every case the rest of body and mind should at least be sufficient to allow the heart to recover the largest amount of reserve force of which it is capable. If the reserve force of the organ is already spent, and, in consequence, breathlessness, palpitation, pain, etc., occur after slight exertion or even during repose, then absolute rest is imperative. On the other hand, young persons with organic mitral disease, especially mitral regurgitation, and others with fatty infiltration of the heart who give evidence of insufficient cardiac reserve force, but who present none of the symptoms of cardiac failure are often benefited by gentle exercise, such as walking on level ground, horseback riding, and playing at golf. In the early stages of degenerative myocardial disease, Swedish exercises and baths containing free carbonic acid gas, such as are used at Nauheim, are sometimes of service, but they must be employed tentatively, their effects upon the patient's pulse and subjective symptoms being carefully observed. In elderly persons with atheroma of the vessels they are usually inadvisable and in cases of angina pectoris and of aortic regurgitation they are contra-indicated. The Oertel treatment, which consistsin walking a certain distance up a gentle incline each day, the distance and pace being gradually increased, is applicable only to cases in which the lesions in the heart are stationary and have not seriously compromised the integrity of the cardiac muscle.

A change of residence to a warm, dry, and equable climate, especially during the winter months, is often very efficacious when the deterioration of the heart muscle is not far advanced, but it is important that patients whose field of cardiac response is much reduced should be spared the trials of a long journey. The great benefit that frequently occurs from a sojourn at Nauheim, Carlsbad, Bedford Springs or some other such resort is probably due more to the rest, good air, freedom from customary vexations, and strict diet and regimen than to any special form of hydrotherapeutic or gymnastic treatment. Whatever climate is selected high elevation should, as a rule, be avoided.

As with rest and exercise so with diet, no hard and fast rules can be laid down. The diet must be carefully adapted, however, to the digestive powers and needs of the system. Rich foods, bulky foods and foods that induce flatulence are clearly inadmissible. The dinner should be at midday

and in all cases the supper should be extremely light. The question of the quantity of food is also one of great importance. In pronounced heart-failure the diet must, of course, be much restricted and the food given in small quantities at comparatively frequent intervals. Degenerative changes in the heart usually occur at a period of life when the amount of food may be considerably reduced without impairing the general nutrition. In certain cardiac cases with edema and chronic nephritis a salt-free diet is efficacious. Balfour, Allbutt and others have dwelt upon the advisability of restricting the amount of liquids taken with meals in cases of cardiac insufficiency. By this means the tension in the venous system may be lowered and the arterial resistance reduced. Judgment, however, must be exercised in the matter of drink, as the amount of fluid required to secure a free evacuation of waste products from the system must vary in different cases.

Tea and coffee should be used sparingly, if at all. Alcohol is better dispensed with. The use of tobacco should be limited, and in pronounced myocardial insufficiency it should be avoided. Excesses of all kinds must be interdicted. The bowels should be normally moved each day. For the purpose, if necessary, a vegetable cathartic should be given at night or a saline in the morning. This may be supplemented from time to time with advantage by a pill of blue mass. Sometimes no single remedy affords such prompt relief from the general distress as a mercurial laxative. If the patient is anemic and his general nutrition poor such tonics as iron, arsenic and strychnin may often be given with advantage. Among special remedies for myocardial insufficiency, digitalis holds the first place and is indicated irrespective of what form of valvular disease may be co-existent. For administration by the mouth a good standardized tincture, a freshly prepared infusion, and powdered digitalis are, as a rule, the best preparations. Nativelle's digitalin and digipuratum are efficient proprietary preparations. One of Nativelle's granules ($\frac{1}{4}$ milligram) is equivalent to about 15 minims (1.0 mil) of the tincture. Digipuratum, which is an alcoholic extract of digitalis, free from digitonin and other inactive substances, is supplied in tablet and liquid forms. Each tablet represents 1$\frac{1}{2}$ gr. (0.1 gm.) of digitalis and 15 min. (1.0 mil) of the liquid is equivalent to 1$\frac{1}{2}$ gr. (0.1 gm.) of digitalis. Liquid digipuratum is a reliable preparation for subcutaneous or intravenous injection.

The good effects of digitalis are brought about in various ways: (1) by reducing the number of cardiac contractions the drug rests the heart and allows the ventricles to become more completely filled, and by increasing the force of the contractions it aids in the more thorough emptying of the ventricles, this combined effect tending to readjust the inequality in the arterial and venous circulations; (2) by thus correcting the abnormal distribution of blood it promotes diuresis and facilitates the removal of dropsical effusions, it improves pulmonary ventilation and oxygenation, and puts the stomach, intestines and liver in a better condition for digestion and absorption and (3) by driving more blood into the coronary arteries it may permanently influence for good the nutrition of the cardiac muscle. Individual actions of the drug add considerably to its value in special conditions. Thus, in auricular fibrillation and auricular flutter its impeding effect upon conductivity serves to prevent many of the excessively numerous contractions arising in the auricle from reaching the ventricle and exhausting it, and in mitral insufficiency with dilatation of the heart digitalis may actually lessen the leakage by producing more powerful systolic contractions, thus reducing the size of the mitral ring.

The best results from the use of digitalis are in cases of auricular fibrillation with dyspnea and a frequent irregular pulse. Whether edema is present

or not is immaterial. In decompensation with a frequent pulse, but a normal rhythm digitalis is less reliable, although it often proves decidedly useful, especially if there is edema and the urine is scanty and concentrated. In both of these conditions the drug should be pushed until the desired effect is obtained or signs of intolerance appear. From 10 to 15 minims of the tincture three times a day will often be sufficient. If nausea, vomiting, diarrhea, headache, or "coupling of beats" occurs the drug should be discontinued and not resumed until the untoward symptom has disappeared. Otherwise it should be continued until the pulse falls to about 70, when it should be stopped for several days and then, if the pulse again becomes frequent, resumed in smaller doses, the amount being changed from time to time in order to determine the exact dose that will control the heart without producing a toxic effect. In auricular fibrillation it is usually, but not invariably, necessary for the patient to continue taking the remedy more or less regularly for the remainder of his life.

Recent studies have shown that quinidin, an isomer of quinin, may actually abolish auricular fibrillation by depressing irritability and conduction in the auricular muscle. Digitalis does not affect fibrillation itself, but it tends to lower the rate of the ventricular contractions and to restore the normal rhythm by depressing the conductivity of the His bundle. Quinidin, however, being depressant to all the cardiac functions, is not so generally useful as digitalis. It is not at all suitable for ambulatory patients and must be used with great care if decompensation is pronounced. Moreover, the drug frequently causes nausea and vomiting and in some instances its effects are distinctly unfavorable. It restores the normal rhythm in from 40 to 50 per cent. of the cases, although a relapse usually occurs in from a few days to several months. Three grains (0.2 gm.) of the sulphate may be given on the first day as a test for idiosyncrasy and then the dose may be gradually increased to 5 grains (0.3 gm.) or, if necessary, to 10 grains (0.6 gm.) three or four times a day. The treatment should be suspended whenever severe headache, precordial distress, palpitation, increased dyspnea, pronounced tinnitus or vertigo, or other untoward symptoms develop. Frey,[1] Schott[2] and others advise against the combination of quinidin and digitalis on the ground that complete heart-block may occur and the ventricle under the depressing effect of the quinidin may be unable to develop an independent rhythm.

In cases of pronounced myocardial degeneration occurring in elderly persons (so-called senile heart) digitalis is not infrequently useless and may be actually harmful, although it is sometimes of service when given in small doses, that is, 5 min. (0.3 mil) of the tincture or ½ gr. (0.03 gm.) of the powdered drug, two or three times a day, or one granule of Nativelle's digitalin at bedtime.

In partial heart-block digitalis should, as a rule, be avoided, but in complete heart-block if there are evidences of cardiac insufficiency it may be employed tentatively. Although the drug has some tendency to excite extrasystoles, the occurrence of these premature beats is not a contra-indication if other conditions are also present in which digitalis is likely to be of service. The height of the blood pressure is immaterial; indeed, in hyperpiesis when the heart is overborne by the excessive labor and gives evidence of yielding, the administration of the drug may prove a valuable addition to eliminative and dietetic measures and rest. Finally, neither aneurysm of the aorta nor arteriosclerosis should be considered a bar to the use of digitalis, if its employment is dictated by changes in the heart itself.

[1] Berlin. klin. Woch., 1918, lv, 417.
[2] Deutsch. Arch. f. klin. Med., 1920, cxxxiv.

When digitalis fails other cardiac tonics rarely succeed. Strophanthus may be tried, but it is less certain of absorption than digitalis, and, therefore, less reliable. Strychnin has been shown to have no important effect upon the heart or bloodvessels in therapeutic doses; nevertheless it is often of value in chronic myocardial disease, especially in the myocardial insufficiency incident to old age. It is likely that the good effects of the drug are due to an improvement in the general muscular tonus brought about by its action on the central nervous system.

*Acute Heart Failure.*—Diffusible stimulants, such as alcohol, ammonia and camphor are of service. Alcohol may be given in the form of brandy or whiskey, in doses of ½ ounce (15 mils), undiluted and preferably hot; ammonia may be used as the aromatic spirit of ammonia in doses of 15 to 30 min. (1.0–2.0 mils) in half a tumbler of water; and camphor should always be given subcutaneously, 15 to 30 min. (1.0–2.0 mils) of a 10 per cent. solution in sterile olive oil being injected at intervals of an hour. In urgent cases a remarkably good effect is sometimes produced by injecting strophanthin into a muscle or preferably into a vein; but under no circumstances should this drug be employed if the patient has been taking digitalis by the mouth within 5 or 6 days. The dose of the official preparation is $\frac{1}{80}$ gr. (0.00075 gm.) in 2 drams (8.0 mils) of normal salt solution. It should not be repeated before 48 hours. Inhalations of oxygen sometimes make the patient more comfortable. Hot applications over the heart act beneficially.

When the right ventricle is greatly distended, as indicated by severe dyspnea, cyanosis, and an increase in the area of cardiac dulness to the right, the abstraction of from 10 to 15 ounces (300–450 mils) of blood from the median basilic vein is very useful.

*Edema.*—In many cases absolute rest, the restriction of liquids to 1500 mils a day, the withholding of salt from the food as far as possible, and the administration of digitalis suffice to remove the edema. Purgatives are of value, but some caution must be exercised in their employment lest they prove exhausting to the patient. The salines and compound jalap powder are usually the best. Diuretics are also useful. The most effective in conjunction with digitalis are caffein, theobromin, theocin and the organic salts of potassium. The following mixture of potassium acetate with the infusion of digitalis often acts well:

℞. Potassii acetatis ..... ʒiii (10.0 gm.)
Infusi digitalis ..... fʒiii (90.0 mils) M.
Sig.—A dessertspoonful three times a day.

Another time-honored remedy is Guy's or Niemeyer's pill, consisting of a grain (0.65 gm.) each of powdered digitalis, powdered squill and blue mass. One pill should be given three times a day, after meals, for several days, the condition of the mouth being carefully observed for evidences of salivation. In some cases caffein or theobromin may be added to the other ingredients with advantage, as in following prescription:

℞. Pulveris scillæ .....
Pulveris digitalis .....
Massæ hydrargyri .....āā gr. xx (1.3 gm.)
Theobrominæ ..... ʒj (4.0 gm.) M.
Pone in capsulas No. xx.
Sig.—One three times a day, after meals.

The application of smooth firm bandages to the swollen limbs sometimes affords much relief. In extreme cases the Karell diet is well worth trying. Briefly stated, it consists in giving 200 mils of milk at intervals of 4 hours

from 8 o'clock in the morning until 8 o'clock in the evening. No other food or liquid is allowed. If there is much thirst the patient may be permitted to rinse out his mouth with water at intervals and if hunger is urgent a small piece of dried toast may be given with each portion of milk. If pleural effusion or ascites is pronounced, and especially if it is causing respiratory embarrassment, paracentesis should be practised. When all other measures have failed recourse may be had to scarification of the most swollen and dependent parts, to the insertion into the subcutaneous tissue on the posterior aspect of the leg on either side of the tendo Achilles of fine silver cannulæ (Southey's tubes) with rubber tubes attached, or to incisions about 2 inches in length behind the inner malleolus on each side. These methods often serve to draw off large amounts of fluid, and thus to relieve the tension in the venous circulation, although they may increase the patient's discomfort and unless carried out with great care as to asepsis are likely to be followed by erysipelatous inflammation.

*Dyspnea.*—Chief reliance must be placed upon those measures that have already been recommended as useful in restoring the balance of the circulation. Dyspnea excited by flatulent distention of the stomach is often relieved by carminatives—Hoffmann's anodyne, spirit of chloroform, spirit of mint, etc. Dry or wet cupping over the back of the chest or venesection may give great relief when there are signs of pulmonary engorgement. Aspiration will be required if there is considerable pleural effusion. When the arterial pressure is high nitroglycerin may prove efficacious. Oxygen is sometimes useful. In severe cases morphin hypodermically (1/8–1/4 gr.—0.008–0.016) is often the only recourse. In paroxysms of acute pulmonary edema (cardiac asthma) occurring at night a combination of morphin and atropin is invaluable.

*Palpitation.*—Rest is often required. Locally, an ice-bag, a sinapism, or a large belladoma plaster may afford relief. Occasionally small doses of aconite are of service. When flatulence is the exciting cause, carminatives will be found efficacious. Palpitation of nervous origin is usually benefited by bromids. If the attacks are very severe and interfere with sleep it may be necessary to use morphin.

*Cardiac Pain.*—Temporary precordial oppression is often relieved by a warm or cold application or a sinapism and the administration of hot whisky, aromatic spirits of ammonia or Hoffmann's anodyne. Dull continuous pain in the upper part of the chest may be favorably influenced by a nitrite or an iodide, even if the arterial pressure is not high. Persistent pain and tenderness over the epigastrium and right hypochondrium, the result of venous stasis in the stomach and liver, may yield to local cupping or leeching and the administration of a mercurial purge. The treatment of angina pectoris is discussed on p. 664.

*Insomnia.*—Restriction of the evening meal to small amounts of the simplest kind of food is helpful. Of the milder somnifacients bromids, (10–20 gr.—0.6–1.3 gm.), veronal (5 gr.—0.3 gm.), and chloralamid (10–20 gr.—0.6–1.3 gm.) are the safest and best. A combination of veronal and codein sometimes acts very well. Bramwell has found paraldehyde useful in cases of myocardial insufficiency with bronchitis. When there is high arterial pressure nitroglycerin alone or in combination with a bromid is often efficacious. On the whole, no remedy is so generally useful as morphin, especially when sleeplessness is associated with pain, precordial distress, anxiety and restlessness. One-sixth of a grain (0.01 gm.) with 1/150 gr. (0.0004 gm.) of atropin is usually sufficient.

*Vomiting.*—This may be due to faulty diet or to digitalis or other drugs. In many cases, however, it is the result of venous stasis in the stomach. In

severe cases it is advisable to rest the stomach. No food should be given by the mouth except iced champagne, whey, albumen water, milk and limewater or peptonized milk.

Calomel is often indicated. Dry or wet cupping is of benefit when the liver is enlarged and tender. Antiemetics are not often efficacious, but bismuth subcarbonate or cerium oxalate may be tried. About 10 gr. (0.6 gm.) of either drug may be given half an hour before feeding. In obstinate cases rectal feeding may become necessary.

## HYPERTROPHY AND DILATATION

Hypertrophy and dilatation of the heart may be conveniently discussed together, since they are so frequently associated and since the causes of the one, with certain limitations, are the causes of the other. Hypertrophy is enlargement due to overgrowth of the muscular tissue. It may involve the whole organ or only certain chambers. Dilatation is enlargement due to overstretching of the muscular tissue. Like hypertrophy it may be total or partial.

**Etiology.**—Overwork of the heart, if long continued, invariably leads to hypertrophy or dilatation, or to both. When, however, the demands are made gradually and are not excessive, and the nutrition of the heart is good hypertrophy is much more likely to be in the ascendency than dilatation.

**Total Hypertrophy.**—This occurs when increased demands are made upon the heart as a whole. Thus, it may result from (1) severe muscular exertion; (2) adherent pericardium; (3) chronic myocarditis; (4) chronic nephritis; (5) prolonged tachycardia, as in hyperthyroidism; (6) immoderate use of alcoholic beverages, especially beer. Although enlargement from these causes is more or less general it is rarely uniform, the left side of the heart usually being more affected than the right.

The hypertrophy occurring with adherent pericardium is probably caused by the extra work arising from interference with the cardiac contractions. It is possible that the hypertrophy which is often observed in chronic myocarditis may be due more to the conditions which have produced the myocardial lesions than to the latter themselves. The hypertrophy resulting from hyperthyroidism is usually ascribed to the persistent tachycardia, but it may be that the thyroid intoxication itself is the more important factor.

The cause of the hypertrophy in chronic nephritis has been the subject of many heated discussions, but these have been productive of no better hypotheses than those which Bright himself formulated. Bright said "the two most ready solutions appear to be either that the altered quality of the blood affords irregular and unwonted stimulus to the organ immediately, or that it so affects the minute capillary circulation as to render greater action necessary to force blood through the distant subdivision of the vascular system."

Bollinger was the first to draw attention to excessive beer-drinking as a cause of cardiac hypertrophy. He attributed this condition to the stimulating effect of the alcohol upon the heart, to the overfilling of the vessels, and to increased nutrition. It may be questioned, however, whether the more systematic examination of the heart would not have shown in many of these cases some evidences of chronic myocarditis. Excessive eating is also given as a cause of cardiac hypertrophy. It probably does not act directly, however but indirectly by disturbing metabolism and thus producing arterial hyper-

tension, arteriosclerosis or nephritis. There is no reliable evidence to support the assumption that heavy smoking, overindulgence in tea or coffee, alcoholism, or sexual excesses are capable of directly causing hypertrophy of the heart.

**Hypertrophy of the Left Ventricle.**—This occurs when there is an impediment to the outflow of blood from the left ventricle, as in (1) aortic stenosis or congenital atresia of the aorta, (2) persistent arterial hypertension, and (3) general arteriosclerosis; or when there is an excessive quantity of blood to be expelled from the left ventricle, as in (4) aortic insufficiency, and (5) mitral insufficiency.

**Hypertrophy of the Right Ventricle.**—This occurs when there is increased resistance to the entrance of blood into the pulmonary artery, as in (1) mitral disease, and (2) certain chronic affections of the lungs, such as pulmonary emphysema and pulmonary cirrhosis; or when there is an excessive amount of blood to be expelled from the right ventricle, as in tricuspid insufficiency.

In the *auricles* hypertrophy is always associated with dilatation. Enlargement of the left auricle is usually dependent upon mitral disease, especially mitral stenosis; and enlargement of the right auricle, upon some disease of the lungs which obstructs the pulmonary circulation, or upon tricuspid stenosis.

**Dilatation of the heart** may precede, accompany, or follow hypertrophy, or it may occur as an independent condition. It results from the same causes as hypertrophy, but it is more likely to prevail when the nutrition of the heart muscle is seriously impaired or when the strain is very sudden and severe. Either of these factors is alone sufficient. Thus, violent physical exertion in persons out of training may cause *acute dilatation*, even in the absence of any degenerative changes in the myocardium, and this condition may also occur in the course of acute infectious diseases if retrograde changes develop in the myocardium, even though the intracardiac pressure is not increased.

Anemia, chlorosis and other states of general malnutrition not rarely lessen the tonicity of the heart muscle to such a degree that simple dilatation ensues. Finally, depressing mental states, such as anxiety and grief, also seem to favor in some subtle way the occurrence of dilatation. Hirsch points out that the number of cases of cardiac insufficiency increased enormously in France and Italy in years of revolution and great public stress.

**Morbid Anatomy.**—Three varieties of cardiac enlargement may be recognized: (1) Simple hypertrophy, a form in which the muscle is thickened but the cavity is of normal size; (2) eccentric hypertrophy, or hypertrophy with dilatation, which is characterized by thickening of the muscle and an increase in the size of the cavity; (3) simple dilatation, in which there is thinning of the muscle and an increase in the size of the cavity. Some writers speak also of concentric hypertrophy, a form in which the muscle is thickened and the cavity is diminished in size; but such a condition is probably always the result of postmortem contraction.

The average weight of the normal heart in the adult is about 300 grams in the male, and 250 grams in the female. In hypertrophy this weight may be increased threefold or even fourfold. In simple and eccentric hypertrophy the wall of the left ventricle, instead of measuring from 10 to 15 millimeters, may measure from 20 to 30 millimeters; and the wall of the right ventricle may be increased in thickness from a normal measurement of from 5 to 6 millimeters to 8 to 10 millimeters. The papillæ and trabeculæ usually

share in the enlargement. The shape of the heart is also changed, according to the seat and degree of the enlargement. When the left ventricle is especially involved, the heart is elongated and extends more to the left. In enlargement of the right ventricle, the heart is increased in its transverse diameter and becomes more globular in form. The color and consistence of the muscle vary with the state of its nutrition. When healthy, the muscle is of a deep-red color and is resistant to the knife.

Microscopically, the individual muscle-cells are increased in size, and their number is probably also increased. Associated with the hypertrophy there is often more or less fibroid change or fatty degeneration.

Simple dilatation is, as a rule, most pronounced in the right ventricle and in the auricles, but it may affect all of the chambers of the heart. The muscular walls are thin, flabby and usually pale, the papillary muscles and trabeculæ are flattened, and the cavities are distended, sometimes to a high degree. The tricuspid and mitral valves are usually rendered incompetent by stretching of the valvular orifices. Frequently blood-clots are found within the cavities and extending into the great vessels. Degenerative changes are almost always found in the heart-muscle.

**Symptoms of Hypertrophy.**—Hypertrophy being a compensatory process may exist indefinitely without causing any subjective disturbance. As a rule, symptoms only arise when the heart is no longer able to meet the abnormal demands that are made upon it. Beginning inadequacy is usually marked by dyspnea, especially upon exertion, a feeling of discomfort in the precordium, throbbing of the vessels and palpitation. With complete failure of compensation the clinical picture becomes identical with that of dilatation.

**Physical Signs.**—Inspection may reveal some bulging and widening of the intercostal spaces in the precordial region, especially in children. The apex beat is displaced downward and outward. Occasionally it is observed as low as the seventh or even the eighth intercostal space, and as far outward as the mid-axillary line. The impulse is usually diffuse and of a "heaving" character. Not rarely systolic retraction is also seen over the lower part of the precordium, even in the absence of pericardial adhesions. As a rule, the pulse is full and strong. The area of cardiac dulness is increased, the extension being chiefly downward and outward in hypertrophy of the left ventricle and in the transverse direction in hypertrophy of the right ventricle. In the absence of any valvular defects, the first sound in the mitral area is loud, dull and somewhat prolonged, and the aortic second sound or the pulmonic second sound, according as the left or the right ventricle is chiefly affected, is usually accentuated. In some cases the second sound is also reduplicated.

In persons with thick chest walls or with pulmonary emphysema ordinary methods of investigation may yield very meagre information; in such cases valuable aid in determining the size and shape of the heart is afforded by the x-ray.

**Symptoms of Dilatation.**—When accompanied by hypertrophy, dilatation may also be a conservative process. Thus, in aortic insufficiency some increase in the capacity of the left ventricle is necessary to accommodate the excessive quantity of blood which is discharged into it in diastole. With the dilatation, however, there must be a commensurate hypertrophy to insure complete emptying of the ventricle in systole, otherwise stasis of blood in the general venous system is inevitable. Dilatation, then, only causes marked disturbances of the circulation when it is unaccompanied by hypertrophy or when accompanied by hypertrophy, if it is in the ascendency.

When dilatation ceases to be compensatory it gives rise to the usual symptoms of cardiac insufficiency (see p. 647), namely palpitation, precordial

discomfort, faintness, dyspnea, digestive disturbances, enlargement of the liver, oliguria, edema, etc.

**Physical Signs.**—The apex-beat may be normal, but usually it is weak and diffuse or altogether invisible. Sometimes it can be seen, but not felt. When the right ventricle is especially involved there may be pulsation in the epigastrium. The pulse is usually of small volume, weak, and accelerated. In many cases it is also very irregular. Distention and pulsation of the jugular veins may be present. Percussion reveals an increase in the area of cardiac dulness in a direction corresponding to the ventricle chiefly affected. If the valves are still competent, the sounds are usually weak, short, and sharp, the first resembling the second in character. In severe cases the pauses between the two sounds may be of equal length, the rhythm resembling the ticking of a watch (embryocardia). At other times, owing to reduplication of one of the sounds, the heart takes on a triple rhythm suggesting the hoof-beats of a cantering horse (bruit de galop). Frequently a blowing murmur, due to relative insufficiency of one of the auriculo-ventricular valves, replaces the first sound in the mitral or tricuspid area. On the other hand, preëxisting murmurs, especially those of mitral stenosis and aortic insufficiency, sometimes disappear when dilatation becomes extreme.

**Prognosis.**—The prognosis of hypertrophy is largely that of its cause. When this can be removed, as in some cases of hypertrophy from overexertion, the return of the heart to its normal dimensions is possible. In the far larger group of cases in which the cause cannot be removed the matter of chief concern is the probable duration of compensation. In forming an opinion the important factors to be considered are the general health of the patient and the nutrition of his heart muscle. So long as these remain good the supervention of dilatation is not to be feared.

Dilatation is dangerous in proportion to its excess over hypertrophy. It is especially grave when it results from disease of the coronary arteries and chronic myocarditis. Acute dilatation often ends in sudden death. Nevertheless, if the cause is remediable complete resolution may occur. This is not rarely the case in overdistention from infectious fevers and severe muscular exertion.

## FATTY INFILTRATION OF THE HEART

Fatty infiltration of the heart consists of an inordinate accumulation of fat upon the surface of the heart and between its muscular fibers. It is simply an excess of the fat which is normally present. The muscle-fibers themselves are not affected, although ultimately, owing to compression, they may atrophy and become the seat of a true fatty degeneration. As a morbid process, its etiology is that of obesity in general.

**Symptoms.**—These are not constant. The patient frequently suffers from some degree of dyspnea on exertion, but this may usually be ascribed to the condition of corpulency rather than to any abnormal state of the heart itself. According to Romberg the fatty overgrowth causes functional disturbance of the heart only when the cardiac muscle becomes too small (relatively) to meet the demands of the increased weight and size of the body. The physical signs are indefinite. The apex beat is feeble; often, indeed, imperceptible; the first sound in the mitral area is usually weak and muffled; and the pulse is, as a rule, of low tension and somewhat accelerated. When the nutrition of the heart muscle itself becomes impaired the symptoms of cardiac

insufficiency, which have been described under chronic myocarditis (see p. 647), gradually supervene.

The **treatment** is that of general obesity, with such modifications as are required by the degree of cardiac weakness.

## FATTY DEGENERATION OF THE HEART

Fatty degeneration is a process of cellular disintegration characterized by the appearance of fat droplets within the affected cells. In the light of recent investigations Virchow's teaching that the substance of the cell is actually transformed into fat must be accepted with considerable reserve. The studies of Rosenfeld[1] and of Leick and Winckler[2] indicate that the fat is transported from distant depots to the injured cells which are incapable of consuming it.

**Etiology.**—The causes of fatty degeneration of the heart may be local or general. The most common local cause is defective circulation in the coronary arteries, the result of sclerotic thickening of these vessels or of chronic valvular disease. The chief general causes are intoxications and cachexias. Thus, it is observed in prolonged infections, in poisoning by phosphorus, arsenic, etc., and in pernicious anemia, leukemia, cancer and other wasting diseases.

**Morbid Anatomy.**—The degeneration may be diffuse or in patches. Even when the cause is general, the left ventricle is usually the part most affected. The heart may be of normal size, though, of course, the tendency is toward dilatation. The muscle has a yellowish color, is soft and flabby, and when cut imparts a greasy feel to the fingers. Microscopically, the muscle cells are found to be studded with fine granules of fat, which for the most part are arranged parallel with the longitudinal fibrils and which may be so numerous as to obscure both the nuclei and the striæ. In the acute infections the fatty changes are associated with cloudy swelling of the fibers and in some cases also with round-cell infiltration of the interstitial tissue (acute myocarditis). In cases due to coronary sclerosis or valvular disease the fibers are frequently atrophied and pigmented and separated here and there by deposits of fibrous tissue (fibroid heart).

**Symptoms.**—In some cases the disease, although extensive, is latent and remains unsuspected until the fatal termination occurs. When symptoms are present they do not differ from those of cardiac insufficiency due to other causes. Dyspnea on exertion, palpitation, a variable degree of precordial discomfort, lassitude, general muscular weakness, dizziness and faintness are the most constant subjective manifestations. Typical angina pectoris is not uncommon and occasionally it is the only symptom directing attention to the heart. Syncopal or pseudo-apoplectic attacks sometimes occur, and if associated with marked bradycardia (Adams-Stokes syndrome), are evidences of heart-block. Toward the end the breathing often becomes intermittent or of the Cheyne-Stokes type. With increasing myocardial weakness and the occurrence of cardiac dilatation congestion of the viscera and edema supervene, but these features are rarely so pronounced as in decompensated valvular disease.

The **physical signs** are indefinite. The cardiac impulse is usually weak and diffuse and when the cavities are dilated the heart dulness is increased.

[1] Zentrabll. f. innere Med., 1901, xxii.
[2] Arch. f. exper. Path. u. Pharm., 1902, xlviii.

The first sound is, as a rule, feeble and muffled. A soft murmur, due to relative mitral or tricuspid insufficiency, is sometimes audible at the apex or ensiform cartilage. The pulse is frequently more or less accelerated, but it may be abnormally slow. It varies in quality according to the associated conditions. In uncomplicated cases it is usually small and of low tension. Cardiac arhythmia is very common and may assume any of its various forms.

**Diagnosis.**—The diagnosis is always more or less uncertain. The evidences of cardiac weakness are usually sufficiently clear, but the differential diagnosis from other forms of chronic myocardial disease is scarcely possible. Simple fatty degeneration may be suspected when a causal factor is present and there are manifestions of cardiac failure, with anginal or syncopal attacks, a feeble impulse, weak sounds, and a small readily compressible pulse, but without general dropsy or other indications of overdistention of the systemic veins.

**Prognosis.**—Fatty degeneration of the heart is always a serious condition, but with the adoption of a suitable mode of life the patient may live many years, and in the acute forms recovery is possible. In many cases, probably the majority, death occurs suddenly in an anginal attack or syncope. Rarely the fatal termination is the result of spontaneous rupture of the heart.

**Treatment.**—The treatment is that of chronic myocarditis (see p. 651).

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## ANGINA PECTORIS

(Stenocardia)

Angina pectoris is a paroxysmal symptom-complex characterized by more or less severe pain in the region of the heart, with a tendency to radiate to the left shoulder and down the left arm, and frequently accompanied by a sense of impending death. It was first systematically described and named by Heberden in 1768, although the symptoms had been recognized by Morgagni in a case of aortic aneurysm as early as 1707. The association of sclerosis of the coronary arteries with angina pectoris was first suggested by Edward Jenner in 1779 in a letter written to Heberden giving an account of John Hunter's case.

**Morbid Anatomy and Etiology.**—The lesion responsible for angina pectoris is usually sclerosis of the coronary arteries with myocardial degeneration or disease of the root of the aorta, just at the openings into the coronary arteries. Some of the worst attacks are due to the occlusion of a large branch of a coronary artery by a thrombus. More rarely autopsy reveals as the chief lesion insufficiency of the aortic valves, aneurysm of the aorta, or adherent pericardium. The vascular changes may be those naturally occurring with advancing years or those brought about by syphilis, gout, chronic nephritis, etc. Syphilis is a very potent factor and in young or middle-aged men the provocative lesion is frequently an aortitis characteristic of this infection. In some cases the excessive use of tobacco or poisoning resulting from focal infection seems to exert an important predisposing influence. Occasionally the attacks follow one of the acute infections, especially influenza. As many patients with coronary sclerosis and seriously damaged hearts suffer no pain, it is evident that some factor other than the organic lesion is necessary to the production of the anginal syndrome. It is probable that this factor has to do with the sensitiveness to stimulation of the central nervous system, which is much more pronounced in some individuals than in

others. If this hypothesis is correct, it affords an explanation of the marked contrast between the incidence of angina in hospital and consulting practice. The frequency with which physicians, lawyers, actors, financiers, and others who are subjected to severe mental and emotional strain are attacked has been commented upon by nearly all writers. In certain individuals the hypersensitiveness of the nervous system appears to be so pronounced that pain is produced with great facility. Indeed, it is possible that in such persons angina may occur in the absence of any appreciable organic change in the heart or aorta. This type of the disease has often been referred to as pseudo-angina, but the term is not a good one, and has been largely superseded by that of *functional angina pectoris*.

Angina pectoris is much more frequent in males than in females. An hereditary predisposition to arterial disease, and incidentally to anginal attacks, is not rarely demonstrable.

In the majority of cases the attacks occur only in response to some *exciting cause*. The most important factor is muscular effort. Walking up hill or against the wind is especially liable to bring on attack. Mental or emotional excitement is also potent. In some patients digestive disturbance is the most common exciting cause, although in this connection it must be pointed out that gastric symptoms, such as belching and nausea, are often the result of an attack rather than its cause. Less frequently patients ascribe their attacks to exposure to cold.

As to the actual *cause of the pain* we are still in doubt. Lancereaux and Peter believed it to be due to a neuritis of the cardiac plexus of nerves. Heberden and Latham ascribed it to cramp of the heart muscle. Traube, Lauder Brunton and many others have held that it is the result of over-distention of the ventricles, and, therefore, of the same nature as that produced by over-stretching of other hollow organs, such as the bowel and bladder. Allbutt for many years has maintained against much adverse criticism that the paroxysms are the direct outcome of disease of the aorta, more especially of that part just above the sigmoid valves, and that the immediate causes of the pain is undue tension of the fibrous outer coat of the vessel. Perhaps the most plausible theory is that of intermittent claudication, originally suggested by Allan Burns, of Glasgow, in 1809, later advocated by Potain, and in recent times ably defended by Osler. According to this theory, pain is due to transient ischemia of the heart muscle, and is likely to occur whenever there is a marked disproportion between the amount of blood needed by the myocardium and that which the coronary arteries are able to deliver to it.

**Symptoms.**—The most constant symptom is paroxysmal pain, which develops suddenly at some point behind the sternum or over the body of the heart and radiates to the left shoulder and thence down the inner side of left arm, sometimes even to the ring and little fingers. The peculiar distribution of the pain is to be regarded as an example of "referred sensation," in the sense of Head and of Mackenzie, irritation arising in the heart or aortic arch, which are insensitive, being conducted to the corresponding visceral segments of the spinal cord, whence impulses arise which are projected along the upper thoracic spinal nerves to the periphery, where they are recognized as pains. In some cases the pain radiates down both arms and occasionally it is felt in the right arm only. In exceptional instances it is most severe in the region of the elbow. The extension of the pain into both arms has been explained on the theory that the peripheral irritation is sufficiently intense to pass over from one side of the spinal cord to the other, and the radiation of the pain into the right arm alone, on the theory that the nerve-endings in the wall of the

right ventricle only have become irritated. As noted by Heberden, the pain in the arm may precede that in the chest for years. The pain is occasionally experienced chiefly in the epigastrium and when this is the case it is likely to be misinterpreted, especially at first, and to be ascribed to some disorder of the stomach. After an attack the skin over the parts in which the pain has been felt is often hypersensitive. It has been shown by Eichhorst and by Gibson that wasting of the muscles and changes in the texture of the skin may also be found at times in the painful regions. The pain varies much, both in degree and character. There may be merely a feeling of oppression about the heart or aching beneath the sternum, or there may be an overwhelming sense of constriction in the chest. If the attack is severe the patient halts and remains motionless. In *angina major* the pain is usually accompanied by a feeling of alarm or dread, and in many cases by a terrible sensation of imminent death. In *angina minor*, the pain is comparatively mild, does not travel far from its starting point, and is not often accompanied by any pronounced feeling of imminent dissolution. Attacks of angina major and of angina minor not rarely alternate with one another in the same subject, and in many cases the mild attacks appear first and later are superseded by the severe ones. The mental anguish is a distinct feature of the syndrome and does not run parallel with the pain. Occasionally attacks occur in which the pain is subordinate and the sense of dying is the conspicuous feature. To seizures of this type Gairdner gave the name *angina sine dolore*.

Except in paroxysms that prove fatal consciousness is not often disturbed. In some instances, however, the heart pang is followed by syncope. Occasionally, too, the same lesion that is responsible for the angina also results in heart-block, and then syncopal, vertiginous, or even epileptiform seizures may accompany the heart pain, but rather as a part of the Adams-Stokes syndrome than of the angina itself.

Vasomotor disturbances are rarely absent in angina major. The skin is usually pallid, cold, and covered with sweat, but sometimes the face is suffused, even congested, and the surface veins are unduly prominent. The blood pressure often rises during the paroxysm, but it may show no material change and occasionally it is actually lowered. In many cases as the symptoms subside, large quantities of pale urine are passed.

Not only may the pain be referred to the epigastrium, but gastric symptoms may be so conspicuous as to lead to errors in diagnosis. Frequently the attack is accompanied by nausea, flatulency, and hiccup, and occasionally vomiting occurs. At the end of a paroxysm there are often noisy eructations of gas, and to these the patient is likely to attribute his relief. The respirations are usually normal throughout, but dyspnea may be present as a result of coincident pulmonary edema.

The attacks may last a few seconds, a few minutes, or several hours, and sometimes they occur in rapid succession over a period of several days. In other cases they are separated by intervals of weeks or months. After severe paroxysms the patient feels exhausted for several hours or for several days. Examination of the patient during the intervals usually, but not invariably, reveals signs of arteriosclerosis or of chronic myocardial disease. Not rarely some enlargement of the heart may be detected, although with the supervention of dilatation and the establishment of relative mitral insufficiency, the anginal attacks may cease (Musser, Broadbent, Allbutt). Other manifestations of cardio-vascular disease may be present; thus, there may be attacks of syncope, of cardiac asthma, or, more rarely, of angina abdominis (see p. 714). Severe paroxysms, the result of cardiac infarcts, are sometimes followed by evidences of circumscribed pericarditis.

**Functional Angina Pectoris (Pseudo-Angina).**—These terms are applied to attacks of cardiac pain, more or less closely resembling those of organic angina, but which are not dependent upon structural disease of the heart or vessels, and which rarely, if ever, prove fatal. Some of these cases are associated with *hysteria;* others are the result of certain *toxic agents*, notably tobacco; and others still appear to be due to a *primary vasomotor instability* (vasomotor angina of Nothnagel[1]). The last form is not uncommon in women during the menopause.

Although the organic and functional forms of angina pectoris sometimes closely simulate each other, the latter may usually be distinguished by attention to the following points: (1) Excepting the toxic form, functional angina is far more common in women than in men; (2) it is often observed at an earlier period of life than the organic form; (3) it is not accompanied, as a rule, by any evidences of arteriosclerosis or of myocardial disease, or by high blood pressure; (4) the attacks frequently arise spontaneously and are rarely provoked by effort; (5) they are of comparatively long duration, often lasting several hours; (6) instead of compelling silence and immobility, they tend to induce emotional excitement and agitation; (7) they are often associated with other neurotic disturbances; (8) if they give rise to apprehension, which is unusual, this sensation is entirely subordinate to the pain; and (9) they are frequently productive of marked palpitation which is somewhat exceptional in the organic form.

**Diagnosis.**—The diagnosis of angina pectoris is not often difficult. Among the conditions which must be excluded are the various colics, gastric, biliary and renal, the crises of locomotor ataxia, aortic aneurysm, intercostal neuralgia, pleurodynia, and cervico-brachial neuritis.

**Prognosis.**—The prognosis of organic angina pectoris is beset with uncertainty. Death may occur in the first attack, or in the second or third, or in one of a series of rapidly recurring attacks. On the other hand, there may be recurring paroxysms over a period of ten years or longer, and occasionally the pains disappear entirely, the patient remaining apparently well for years. In the syphilitic form of the disease the outlook is more hopeful, although by no means wholly favorable. In many cases of syphilitic aortitis even the most energetic treatment is without avail. The prognosis, generally speaking, is most unfavorable if the attacks occur during sleep or when the patient is quiet, or if pain is very easily provoked by exertion. Much depends, however, upon the effect of rest and the removal of secondary influences, such as excessive smoking, intemperance in eating, and poisoning, the result of focal infection. If little or no improvement follows treatment along these lines the condition must be regarded as a very serious one. The occurrence of high blood-pressure during the paroxysms does not make the outlook any worse, but persistent high tension between the attacks, especially if there is evidence of chronic nephritis, should make the prognosis guarded. The presence of valvular disease does not in itself materially increase the gravity of the prognosis, but it is scarcely necessary to add, indications of myocardial insufficiency make the outlook more gloomy. The appearance of cardiac asthma is especially ominous.

**Treatment.**—The treatment of angina pectoris in the intervals between the paroxysms is for the most part that of the arterial or cardiac disease of which the angina is only a symptom. Secondary influences which may have been exhausting the heart itself or irritating the nerve centers should be sought for and removed. In all cases it is imperative that the patient should lead a quiet, easy life, should avoid as far as possible all mental and physical excite-

[1] Deutsch. Archiv. f. klin. Med., 1867, Bd. iii.

ment, and should abstain from the use of tobacco and alcohol, and, as a rule, from that of coffee. The element of rest is of vital importance, but good judgment is required in determining how complete it shall be and for what period of time the inactivity, relative or absolute, shall be enforced. If the attacks are frequent and easily provoked, or if there is much breathlessness, the patient should be advised to keep in bed. On the other hand, if the seizures do not occur frequently or readily, and there is no indication of cardiac exhaustion, exercise need not be altogether foregone. Walking is the best form of exercise, but it should be on flat ground, and never against a strong wind. Gentle massage, and even a few passive movements, may sometimes be attempted even in bedridden patients, but resistance exercises, as well as the Nauheim baths, are inappropriate.

The question of diet is scarcely less important than that of exercise. Small meals of readily digested food are to be recommended. Meat, as a rule, should be used sparingly. Hot breads, fried meats, greasy pastry, coarse vegetables, and highly seasoned dishes are inadmissible. The evening meal especially should be light. Muscular exercise and mental excitement of any kind after meals are particularly injurious. The bowels should be kept regularly open, mild aperients being used for the purpose if necessary.

Between the attacks no drug is so generally useful as potassium iodid, although the manner of its action is not definitely known. It is most effective, of course, in cases of syphilitic origin, but it is not without a beneficial action in angina from other causes. However, in aged persons, in whom the cardiac pain is but one of the manifestations of the involutionary changes taking place in the arteries, the iodid is of little value. To be effectual in any case the drug must be given for a considerable period of time. Except in case of syphilis, doses of 10 grains (0.6 gm.) three times a day, are usually sufficient. Next to the iodid no remedy is so serviceable as nitroglycerin. It often does good even when the blood pressure is not high. It acts favorably by relaxing the coronary arteries, although by depressing the vagus it tends also to improve the tonicity and contractility of the heart. Nitroglycerin and other vasodilators must be used with considerable caution, however, in cases of chronic nephritis with hypertension. In cases in which excessive nervous irritability is a conspicuous feature, bromids in full doses are indispensable. Digitalis has no place in the treatment of angina pectoris itself. It should be reserved for the menacing effects of cardiac dilatation. Alone or in association with theobromin it is also of service in cases of hypertension when the urine becomes scanty and uremia seems imminent. In anemic and debilitated patients tonics, especially arsenic and iron, are very useful. Finally, any constitutional disease that may be present, such as gout or syphilis, must receive appropriate treatment. Arsphenamin was formerly believed to be contraindicated in cardiovascular syphilis, but it is now known that if the drug is given at first in small doses (0.2 gm.) and the amount cautiously increased, it is safe and often of value. Its use should always be followed by that of mercury and an iodid.

*The Attacks.*—When attacks are brought on by indigestion, they can frequently be staved off by the timely use of a brisk mercurial or saline laxative. Flatulency should be met by the administration of a stimulant carminative, such as whisky, aromatic spirit of ammonia, or spirit of ether. For the relief of the pain no remedy is so useful as amyl nitrite. In the majority of cases a mere whiff of this speedily arrests the paroxysm. The patient should carry the remedy on his person in a small vial or better in the form of glass "pearls," containing from 3 to 5 minims (0.2–0.3 mil), which can be broken in a handkerchief and the vapor inhaled, as soon as he perceives the pain. For

mild attacks a drop of the spirit of nitroglycerin on the tongue is sometimes sufficient. If the paroxysms are severe and prolonged, morphin and atropin should be given hypodermically. If amyl nitrite and morphin fail, recourse may be had to the inhalation of chloroform, but the use of this drug is attended with a certain degree of risk. It is especially dangerous if the blood-pressure is low and symptoms of shock accompany the pain. The application of a mustard-plaster to the precordial region is sometimes useful in cases in which the attacks are prolonged and occur in rapid succession. Cardiac depression following a paroxysm should be combated by such drugs as camphor, strychnin, and caffein, and if necessary, by the inhalation of oxygen. After severe attacks it is necessary to enjoin rest in bed for several days.

## IRRITABLE HEART

**(Irritable Heart of Soldiers; Neurocirculatory Asthenia; the Effort Syndrome)**

This is a symptom-complex consisting of various neurocirculatory disturbances, resulting from hardships and anxiety, and especially from the harsh experiences of warfare. It was first accurately described in 1871 by Da Costa,[1] who saw many examples of it among the soldiers during the American Civil War. Since then many references have been made to it, and during the recent European War cases were so numerous in both the Allied armies and in those of the Central Powers that more than two hundred papers were published on the subject. Lewis[2] states that of some 70,000 soldiers returned to British Hospitals on account of cardiac insufficiency, approximately only 10 per cent. had structural heart disease. Irritable heart, however, is not peculiar to military life, and at the draft it was a common cause of rejection. It develops more readily in persons who from heredity or environment are naturally weak and timorous, but under prolonged stress even the most robust and fearless may succumb. In soldiers heavy equipment, long marches, insufficient or indigestible food and nostalgia favor its occurrence. The condition is apparently not an expression of hyperthyroidism, as some writers have suggested, but rather a "subconscious defence reaction to an intolerable situation."

**Symptoms.**—The symptoms resemble those occurring in a healthy person who has excited himself to the point of exhaustion, hence the term "effort syndrome" used by Lewis. The most constant symptoms are precordial discomfort or pain, shortness of breath or a sense of suffocation, palpitation, headache, dizziness, rapidly succeeding blushing and paling of the skin, sweating of the extremities and ready fatigue under mental or physical exertion. With these manifestations there may be also disturbed sleep, syncopal attacks, vague pains in the back and limbs, and various gastro-intestinal neuroses.

The **physical signs** are fairly uniform and consist of an anxious expression, coarse trembling of the extremities, exaggeration of the tendon reflexes, cold, moist hands, which become blue when dependent, an increased pulse rate (90–130 per minute) with abnormal response of the heart to exertion, rapid and shallow respiration, a precordial area of hyperesthesia, a diffuse and forcible cardiac impulse, and accentuation of the heart-sounds. The heart is of normal size, the blood-pressure in repose is usually normal, but the systolic pressure is often unduly elevated by exertion, arhythmia,

[1] Amer. Jour. of Med. Sci., Jan., 1871.

[2] The Soldier's Heart and the Effort Syndrome, 1919.

except of the sinus type, is uncommon, and the heart-sounds are, as a rule clear, although not rarely there is a systolic murmur or a slight roughening of the first sound at the apex.

**Diagnosis.**—If a murmur is present at the apex the condition may readily be mistaken for *mitral valvular disease*. The latter may be excluded, however, if there is no history of rheumatism, chorea or other infection likely to cause endocarditis, if the apex is not displaced outward or downward, if the heart is not enlarged, if the murmur is not propagated beyond the mid-axillary line, and if there is no disproportionate accentuation of the pulmonary second sound. *Hyperthyroidism* may also be closely simulated but in irritable heart the thyroid gland is not usually enlarged, the tremor is coarse, there is no genuine exophthalmos, the increased pulse and rapid breathing subside during absolute rest and sleep, there is mental lethargy rather than alertness, and the basal metabolism is not above normal (Peabody, Wearn and Tompkins[1]).

**Prognosis.**—Unless the condition is very severe and is based upon a pronounced neuropathic disposition, the outlook is favorable.

**Treatment.**—Agreeable sanitary surroundings, wholesome food, graduated exercises, suitable amusements, and psychotherapy in the form of encouraging suggestions and hopeful assurances, are the important factors in treatment. Drugs are of little value, but laxatives may be used for constipation, iron for anemia, and bromids for troublesome insomnia. Neither digitalis nor aconite has any effect upon the tachycardia.

## ANEURYSM OF THE HEART

**Saccular aneurysm of the wall of the heart** is usually caused by the dilatation of a circumscribed area that has been weakened by fibroid change, the result of sclerosis of the coronary arteries, gummatous infiltration, or, very rarely, a wound. *Acute aneurysm* is an occasional sequel of ulcerative myocarditis. The anterior wall of the left ventricle near the apex was the seat of the dilatation in 55 of 87 cases collected by Pelvet.[2] The size of the sac varies from that of a cherry to that of an orange. Thrombi are usually found in the interior; they may be soft and granular or firm and laminated. The terminations are variable. In some instances, after reaching a certain size, the aneurysm remains stationary. Wilks[3] reports a case in which a cardiac aneurysm the size of a pigeon's egg had become completely filled with a firm clot. Very often death results from cardiac insufficiency, to which, however, the aneurysm may be only contributory. It is remarkable how rarely rupture occurs; only 7 of 90 cases collected by Legg[4] having ended in this way. Sudden death from embolism of a coronary artery is a possible termination.

*Dissecting aneurysm of the heart* is an interesting form. It usually originates at the aortic orifice from ulcerative processes or traumatic rupture, and extends into the periaortic space of Vestberg. Aneurysms in the beginning of the aorta occasionally extend into the wall of the heart and become dissecting by secondary rupture. In 1897 Vestberg[5] collected from the literature 60 cases of cardiac dissecting aneurysm.

[1] Medical Clinics of North America, Sept., 1918.
[2] Des Aneurysmes du Cœur, Paris, 1867.
[3] London Path. Trans., vol. viii, 1878.
[4] Medical Times and Gazette, vol. ii, 1883.
[5] Nordiskt Medicinskt Arkiv., 1897, B. vii, Nos. 26–30.

**Aneurysms of the valves** are usually the result of ulcerative endocarditis, although they may be caused by atheroma. The bulgings are more or less spheric and those of the aortic segments protrude into the ventricle and those of the mitral segments into the auricle. Rupture of the valve, resulting in extensive insufficiency, is a common termination in acute cases. When large, valvular aneurysms sometimes obstruct the orifice at which they are located; small dilatations frequently give rise to no special disturbance, the endocarditis with which they are associated running its usual course.

**Aneurysms of the coronary arteries** are rare. Either vessel may be affected. The most common site of the dilatation is near the origin of the artery from the aorta. In 11 of 19 cases tabulated by Capps[1] death resulted from the rupture of the aneurysm into the pericardium.

The diagnosis of cardiac aneurysm is scarcely possible, the symptoms being indistinguishable from those of the primary disease.

## RUPTURE OF THE HEART

Spontaneous rupture of the heart is of rare occurrence. It is more common in men than in women. It seems to be disproportionately frequent among the insane. Of 115 cases tabulated by Odriozola,[2] in 94 the age was over 60, and in only 9 was it under 50. The accident has always occurred in a heart weakened by some pre-existing disease. Fatty degeneration with stenosis of the coronary arteries is the lesion usually encountered. Among the less frequent causes may be mentioned anemic necrosis from occlusion of one of the coronary arteries, suppurative myocarditis, gumma, neoplasm, aneurysm, and echinococcus cyst. Sometimes the rupture occurs during complete repose, as in the classical case of George II, but far more frequently physical exertion or mental excitement is the determining factor. Thus, it has occurred during severe muscular effort, vomiting, coughing, defecation or coitus. In one instance it was caused by the passage of a stomach-tube, and in another by catheterization. The rent in most cases is located on the anterior aspect of the left ventricle near the apex. The amount of blood found in the pericardium varies from a few ounces to a quart or more. In 71 of 100 cases collected by Quain[3] death was instantaneous. Sometimes, however, the rent is temporarily filled by blood-clot, and life is prolonged for several hours or even several days. Barth[4] cites a case in which the patient lived ten days after perforation took place. Such remarkable prolongation of life after rupture of the heart, as well as the trivial character of the injury that may lead to the accident, makes the condition especially interesting from a medicolegal viewpoint.

**Rupture of the Valves.**—Valves, the seat of sclerotic changes, are sometimes torn by direct or indirect violence. The aortic valves are most frequently affected, next the mitral, and then the tricuspid valves. In mitral lesions the segments do not give way, but the chordæ tendineæ.

**Symptoms.**—The symptoms of cardiac rupture, when life is not immediately terminated, are severe pain, dyspnea, syncope and collapse. Epileptiform convulsions have occurred in some cases. A rapid increase in the area of cardiac dulness and muffling or effacement of the heart sounds are

[1] American Jour. of Medical Sciences, Sept., 1899.
[2] Quoted by Letulle: Anatomie Pathologique, 1897.
[3] Lancet, vol. i, 1872.
[4] Archiv. Général., 1871.

significant signs of hemorrhage into the pericardium. Valvular ruptures frequently produce a loud double bruit.

Spontaneous rupture of the wall of the heart is invariably fatal. Occasionally patients live for several years after rupture of one of the valves.

## ENDOCARDITIS

**Varieties.**—Inflammation affecting chiefly the valves of the heart is known as *valvular endocarditis*, while that affecting the lining of the auricles and ventricles is referred to as *mural endocarditis*. In the great majority of cases the process is chiefly valvular. Endocarditis, according to its course, may be acute, subacute, or chronic. It is customary to classify cases of *acute endocarditis* as (1) simple or benign and as (2) malignant or ulcerative. Although such a division is not justified either by etiologic or pathologic differences, it may still be retained to designate the extremes of a process which manifests all degrees of severity according to the variety of the infecting agent, the virulence of the infection, and, perhaps, the resistance of the tissue to infection. An etiologic classification would be entirely satisfactory, but this is not yet possible.

A number of bacterial types of the disease, however, have been definitely recognized; thus, we speak of rheumatic endocarditis, streptococcus hemolyticus endocarditis, gonococcus endocarditis, etc.

*Subacute endocarditis*, or endocarditis the duration of which is measured by months instead of by days or weeks, is due in the vast majority of cases to Streptococcus anhemolyticus, although occasionally the infecting agent is the influenza bacillus or some other organism. In almost all instances the infection is engrafted upon a previously damaged valve. Anhemolytic streptococcus endocarditis sometimes persists for two years or more, in which case it may, properly be termed chronic, and rarely it runs an acute course.

Endocarditis is said to be *chronic* when its duration is measured by years. Only a few of the persistent or permanent valvular defects are examples of chronic endocarditis, although this term is often loosely applied to the majority of them. The lesions of the valves remaining after acute endocarditis are in many instances but the cicatricial scars of an obsolete process. Primary sclerotic thickening of the endocardium is common and frequently results in incompetence of the cardiac valves or stenosis of the orifices, but it is a chronic degenerative process rather than a chronic inflammatory one. In many cases of mitral and tricuspid insufficiency there are no inflammatory changes in the valve segments themselves or in the adjacent tissues, but the cause of the leakage is a lack of contractility in the muscular ring or enlargement of the orifice due to dilatation of the ventricle. True chronic endocarditis is sometimes observed in infection of the valve segments with anhemolytic streptococci, the duration of the disease being measured by years instead of by weeks or months, as is usually the case. Again, in some cases of acute simple inflammation of the valves arising from a local focus of infection recurrences follow each other so rapidly that it seems justifiable to refer to the condition as one of chronic endocarditis.

### ACUTE SIMPLE ENDOCARDITIS

**Etiology.**—Acute simple endocarditis is probably always secondary to an infectious process elsewhere in the body. By far the most frequent cause of

the disease is *acute rheumatism*, the etiologic agent of which is still undetermined. Although rheumatism so mild as to be readily overlooked is capable of exciting endocarditis, the latter is more likely to develop when the general infection is severe and several joints are involved. The first attack of rheumatism appears to be the most dangerous in this respect and the younger the subject the greater is the liability to cardiac disease. The frequency of endocarditis in rheumatism has been variously estimated; probably a percentage between 40 and 50 would not be far from correct. The mitral valve is most frequently affected and the valves of the right heart usually escape. Only occasionally does rheumatic endocarditis pursue a malignant course.

*Chorea* is probably the next most important cause of the disease. Osler found vegetations in 62 of 73 fatal cases of chorea. Endocarditis from this cause is usually of the simple type. Other infections which seem to be more or less closely related to rheumatism, such as *acute tonsillitis* and *arthritic purpura*, may also produce simple endocarditis. *Pneumonia*, *septicemia* and the *exanthemata* are responsible for a certain number of cases. *Acute gonorrhea* is an occasional cause, the disease being incited by the gonococcus itself or by pyogenic cocci which have invaded the organism through the urethral lesion. True gonococcal endocarditis is usually malignant, and in a large proportion of cases attacks the aortic valve. That *local foci of chronic septic infection*, such as may occur in the tonsils, teeth, gall-bladder, etc., are not infrequent causes of acute, subacute, and chronic endocarditis is now generally recognized. The *terminal infections* to which many sufferers from chronic nephritis, carcinoma, tuberculosis and diabetes ultimately succumb sometimes express themselves locally as an endocarditis. A few cases of true *tuberculous endocarditis* have been reported. Finally, *contusions* of chest, even in the absence of external wounds, may occasionally produce in the endocardium a *locus minoris resistentiæ* in which bacteria present in the circulation find a nidus and set up an inflammatory process.

Acute simple endocarditis may occur at any age; even the fetus is not exempt. Children and adolescents, however, owing to the prevalence among them of rheumatism, chorea and other acute infections are more frequently affected than adults. Hearts in which the valves are already damaged are more vulnerable than those that are sound.

**Morbid Anatomy.**—Except in fetal life, acute simple endocarditis much more frequently affects the mitral and aortic valves than those of the right side of the heart. The lesions are most marked where there is the greatest friction, that is on the aspect facing the direct blood stream, and along the line of maximum contact, or about 2 mm. from the free margin of the cusps. In severe cases other parts of the endocardium, especially the chordæ tendinæ may also be involved. The affected area first becomes rough and opaque from necrosis of the endothelium; later, owing to this endothelial defect a deposition of fibrin occurs in the form of bead-like excrescences or vegetations (thrombi). The latter measure from 1 or 2 mm. in mild forms to 3 or 4 mm. in severe forms of the disease. As the process continues young connective tissue cells penetrate the thrombotic mass and gradually transform it into scar tissue, which in contracting often so deforms the valves as to make them in one case obstructive to the blood flow and in another incompetent to close the orifice over which they preside. Finally, in advanced cases, calcification of the indurated tissue may occur, rendering the valves still less efficient. Even before they have undergone organization, the vegetations may cause insufficiency of the valve by preventing accurate coaptation of the leaflets. In some cases the inflamed cusps adhere to one another, thus producing marked obstruction.

**Associated Lesions.**—Myocarditis is probably present to a greater or less extent in every case of endocarditis. When marked it is a much more important factor in disturbing the cardiac mechanism than the valvular defect itself. Pericarditis is also common. Infarcts may occur in the spleen, kidneys, brain or elsewhere in consequence of fragments of thrombi being carried into the circulation and deposited as emboli.

**Bacteriology.**—Various microörganisms are concerned in the production of acute endocarditis, but it is usually difficult to demonstrate their presence in the simple form of the disease. Especially important are the streptococci, staphylococci, and pneumococci. The question of the specificity of the micrococci described by Poynton and Paine, Beattie and others in connection with rheumatism still remains unsettled. The bacteria responsible for acute endocarditis probably invade the valves directly from the surface, as Klebs and Virchow taught, and not by way of the capillaries, as these vessels, according to recent observations (Coen and von Langer) do not extend beyond the base of the valves.

**Symptoms.**—In a large proportion of cases subjective symptoms are absent or are so obscured by those of the disease which has excited the endocarditis that they escape recognition. Moreover, when symptoms are present, they are usually the expression of a coexisting myocarditis rather than of the valvular lesion itself. There may be a rise of temperature of one or two degrees above that previously existing, palpitation, and slight dyspnea. Marked dyspnea that cannot be accounted for by conditions outside of the heart is indicative of extensive myocarditis or of pericarditis with effusion. Cases on the borderland between simple and malignant endocarditis are frequently characterized by a persistent remittent fever, free perspiration, and pallor. Embolic processes sometimes occur, in the spleen, kidneys, lungs or brain, but they are far less common than in the ulcerative form. There results are purely mechanical.

**Physical signs** usually afford the only reliable evidence of acute simple endocarditis. In many cases the pulse is accelerated out of proportion to the degree of pyrexia. Irregularities of the pulse, too, are often noted and are to be ascribed to coincident changes in the myocardium. A tumultuous action of the heart is not uncommon and even in the absence of other signs is of considerable significance. Percussion, at first, rarely elicits any change in the area of cardiac dulness, later, however, some enlargement of the heart may be detected, if the lesions are sufficiently severe. In the majority of cases auscultation reveals at the apex, less frequently at the base, a muffling and prolongation of one of heart sounds, usually the systolic. In a variable time this imperfection develops into a more or less distinct murmur, which, as a rule, is of a soft blowing character. In the case of a mitral lesion the pulmonic second sound is often accentuated. Occasionally, even though the vegetations are extensive, no abnormality in the sounds can be detected. In such cases an absolute diagnosis is impossible.

**Diagnosis.**—The mere occurrence of a systolic murmur in the course of an infectious disease is by no means a certain indication of acute endocarditis. Such a murmur is often caused by enlargement of the mitral ring, due to relaxation of the ventricular wall, and in time disappears. Before venturing a positive opinion every feature of the case should be carefully considered. Not infrequently it is necessary to reserve judgment for several weeks. A diastolic murmur is, as a rule, an indication of permanent organic disease. Dyspnea, precordial distress, a rapid irregular pulse, and an increase in the area of cardiac dulness are, of course, evidences of myocarditis rather than of endocarditis.

**Prognosis.**—Although there is rarely any danger to life in acute simple endocarditis, the ultimate prognosis must remain more or less doubtful. Almost invariably the disease results in a permanent valvular defect, the gravity of which will depend upon the site and extent of the lesion and still more upon the degree to which the myocardium has been affected. It must be borne in mind, also, that damaged valves are more prone to infection than normal ones, and in consequence recurrences of endocarditis are common.

**Treatment.**—This is mainly that of the primary disease and of acute myocarditis (see page 644).

## MALIGNANT ENDOCARDITIS

### (Ulcerative Endocarditis; Acute Septic Endocarditis)

In this form of acute endocarditis, which was first accurately described by Kirkes[1] in 1853, the infection, owing to its extreme virulence, progresses indefinitely, the reparative processes being entirely subordinate to thrombus formation and necrosis of the tissues.

**Etiology.**—Malignant endocarditis is observed most frequently in persons between 30 and 45 years of age and is uncommon in children. In a large percentage of cases (61 of 69 cited by Coupland, three-fourths of those analyzed by Osler, and in 108 and 118 of Horder's cases) it attacks valves that are already the seat of chronic sclerotic changes. Lowered vitality from overwork, alcoholism, debilitating disease, etc. seems to exert a predisposing influence. In the large majority of cases the disease is secondary to septicemia from open wounds, puerperal fever, erysipelas, gonorrhea or pneumonia. Less frequently it occurs in the course of a specific fever, such as scarlatina, diphtheria, measles or influenza. Only in exceptional cases is it the result of rheumatism or chorea. Occasionally it is associated with furunculosis, ulceration of the skin, or focal suppuration in the middle ear, or elsewhere. In rare instances the infection-atrium is not demonstrable.

Microörganisms are present in large numbers in the endocardial lesions and frequently they may be isolated from the blood during life. The Streptococcus hemolyticus is by far the most common causative agent, but not rarely the pneumococcus, gonococcus or staphylococcus is the organism concerned in the process. In a few instances the diphtheria bacillus, influenza bacillus, or meningococcus seems to have been responsible for the lesions.

**Morbid Anatomy.**—The left side of the heart is more frequently affected than the right, although the latter is involved in a larger proportion of cases than in acute simple endocarditis. Mitral lesions predominate, but in about one-half the cases two or more valves are affected. The vegetations, as contrasted with those of simple endocarditis, are luxuriant, in some instances, especially of gonococcus endocarditis, attaining the size of a large cherry. Occasionally they are so large that they virtually occlude the valvular orifice. They are more friable, as a rule, than those of simple endocarditis and show a greater tendency to disintegrate and produce emboli. In many instances they spread to adjacent parts, such as the chordæ tendinæ, the wall of the auricle or ventricle, or the aorta. Accompanying the vegetations there is always more or less necrosis or ulceration of the valve itself and in some cases the destructive process penetrates so deeply that it results in rupture of the chordæ tendinæ, aneurysm or perforation of the valve segments, aneurysm of the aorta, or abscess formation in the wall of the heart.

**Symptoms.**—The symptoms of acute malignant endocarditis are very variable; its onset may be abrupt or insidious, and its course may be measured by days, weeks or months. In the majority of cases three groups of symptoms may be recognized: the toxemic, the cardiac, and the embolic. Fre-

[1] Edinburgh Med. and Surg. Jour., vol. xvii, 1853.

quently, however, one of these groups dominates the clinical picture, the others being subordinate or wholly suppressed.

Among the *toxic symptoms* fever is the most constant. It may be high and continued, but usually it is moderate in degree and irregularly remittent, or intermittent. In rare instances the disease is afebrile. Profuse sweats and repeated rigors are not uncommon, especially in the cases characterized by marked fluctuations in the temperature. Nervous symptoms are rarely absent. These may consist merely of headache, restlessness and anxiety, but in the later stages muttering delirium frequently develops, and ultimately there may be stupor or actual coma. The pulse is compressible, usually frequent, and not rarely irregular. Occasionally, as a result of heart-block, it is in frequent. Gastro-intestinal symptoms are not often conspicuous, but there may be persistent vomiting and diarrhea. In many cases the tongue becomes dry and brown and sordes form upon the lips. Cutaneous rashes, usually of an erythematous type, are not uncommon. Even in cases that are not rheumatic the joints may be painful and tender. The spleen is often enlarged. The urine usually contains albumin and a few hyaline casts. As the intoxication continues general weakness and emaciation develop, and frequently profound anemia becomes an obtrusive feature. An examination of the blood usually reveals in addition to a deficiency in the erythrocytes and hemoglobin, a moderate leucocytosis of the polymorphonuclear type. In a large proportion of cases the causative microörganisms can be cultivated from the blood.

The *cardiac phenomena* are much the same as those of simple endocarditis. In most cases a more or less distinct murmur can be heard over the mitral or aortic area. Marked variations in the quality and intensity of the murmur from day to day are often observed and are somewhat significant. Preëxisting murmurs usually change their character and in many instances there are evidences that the valves are being attacked one after another. Occasionally, the heart sounds remain normal until the end. A sense of oppression over the heart is common, but actual pain is rare. An increase in the area of cardiac dulness is often apparent. Dyspnea may not be marked unless there are pulmonary complications.

The *embolic phenomena* vary widely according to the part affected. Minute hemorrhagic extravasations (petechiæ) into the skin, conjunctivæ and buccal mucous membrane are especially common and are of considerable diagnostic importance. They are usually ascribed to emboli, but it is possible that in some instances they are due to degeneration of the capillary endothelium of bacterial origin. Simple infarcts in the kidneys and spleen may be unattended by symptoms; in some cases, however, they are manifest in the former by hematuria or a sudden increase of the albuminuria, and in the latter by enlargement of the organ and acute pain (perisplenitis). Embolism in the brain may give rise to sudden paralysis, with or without unconsciousness, to aphasia or to coma; in the retina, to blindness; in the intestine, to intense colicky pain, tympanites, and loose bloody stools; in the lungs, to pleuritic pain, dyspnea, cough and bloody expectoration; and in the larger arteries of the extremities, to gangrene or infective aneurysm. Among other complications that are sometimes the result of embolism may be mentioned meningitis, purulent panophthalmitis, parotitis and arthritis. Meningitis is not uncommon, especially in cases of pneumococcus origin, in which it may be either secondary to the endocarditis or the direct result of the primary pneumonia. As the emboli are of an infective nature, the infarcts produced by them are not rarely followed by abscess formation. In some cases, even though the vegetations are accompanied by extensive ulceration, embolism does not occur.

**Clinical Types.**—In a certain number of cases the clinical picture resembles that of typhoid fever (*typhoid type*), the cardiac symptoms being absent or ill-defined, and a continued fever, increasing weakness, somnolence, muttering delirium, and a dry and brown tongue being the obtrusive features. In another group of cases the predominant symptoms are those of a general septicemia or pyemia, in which the heart has become incidentally involved (*septic type*). This type is usually seen in connection with puerperal fever or a suppurating wound. In other cases there are evidences of acute inflammation in a heart that is already the seat of chronic valvular disease and from the onset the cardiac phenomena, such as palpitation, precordial discomfort, dyspnea, etc., predominate (*cardiac type*). Finally, there are cases in which the cardiac symptoms are completely overshadowed by those of an acute cerebral disease, especially meningitis (*cerebral type*). This type is most often found in association with pneumonia. In more than one instance the patient has been sent to an insane asylum, the case having been regarded as one of acute mania.

**Course and Terminations.**—Acute malignant endocarditis may terminate fatally within a few days or it may continue for weeks or months. The course of the disease may be steadily downward or it may be interrupted by periodic remissions. In the vast majority of cases the disease ends fatally, this event being usually the result of exhaustion or of some secondary lesion, such as meningitis, pericarditis, pulmonary edema, or infarction of the brain, lungs or intestine. Occasionally diarrhea of a choleraic type brings about a fatal collapse. A rare termination is rupture of the heart from mural ulceration. Bristowe cites a case in which the cause of death was obstruction of both femoral arteries by large emboli. Sudden death from embolism of one of the coronary arteries has also been reported. Very rarely, especially in gonococcal cases, the disease eventuates in recovery, but with permanent damage to the valves.

**Diagnosis.**—The diagnosis of acute malignant endocarditis may be easy or extremely difficult. Especially significant is the sudden appearance of an endocardial murmur or the occurrence of marked changes in a preëxisting murmur in association with persistent pyrexia, chills, sweatings, progressive anemia, and a petechial eruption or other embolic phenomena. In *simple endocarditis* the fever is neither so high nor so prolonged, prostration is less pronounced, rigors and sweating are absent, embolism is of infrequent occurrence and bacteria can rarely be demonstrated in the blood. *Typhoid fever* and malignant endocarditis have many clinical features in common; but indicative of the former are a gradual onset, a regular temperature curve, a roseolar rash, abdominal tenderness, loose ochre-colored stools, hypoleucocytosis and a positive Widal reaction, and in favor of the latter are an abrupt onset, irregular remittent or intermittent fever, the presence of an endocardial murmur changing in quality and intensity from day to day, precordial discomfort, tumultuous action of the heart, petechiæ or other embolic phenomena, and leucocytosis. Not rarely a blood culture will afford decisive information. The differentiation of malignant endocarditis from *acute miliary tuberculosis* is sometimes difficult, but ordinarily the presence of a primary tuberculous lesion in the lungs, lymph-nodes or bones, hypoleucocytosis and the absence of cardiac signs, petechiæ, etc. point to tuberculosis. In some cases a blood culture or lumbar puncture will decide the question.

**Treatment.**—The treatment is largely that of the initiating septic infection. In some cases of streptococcal origin an anti-serum seems to have been of service, but generally the results of this method of treatment have been

unfavorable. Autogenous vaccines have not proved successful. The administration of quinin in moderate doses has frequently been recommended. Symptoms of cardiac failure should be treated on the lines laid down for acute myocarditis (see p. 644).

## SUBACUTE MALIGNANT ENDOCARDITIS
### (Subacute Infective Endocarditis)

**Etiology.**—This form of the disease is much more common than acute malignant endocarditis. In the vast majority of cases it is due to a non-hemolytic streptococcus (S. viridans), but the influenza bacillus and the gonococcus are both capable of producing it. The disease occurs most frequently in early adult life and is comparatively rare in childhood and old age. It nearly always attacks valves that are already damaged, although the defects may have been too slight to produce symptoms. The primary infection originating the disease may be in the tonsils, gums, roots of the teeth, intestines, gall-bladder, uterus or elsewhere, but wherever its site, the process is usually one that has caused little or no local disturbance. This is in contrast with acute malignant endocarditis, which is almost always associated with a very active focus of infection.

**Morbid Anatomy.**—The mitral or the aortic valve is usually affected. The lesions are similar to those of acute malignant endocarditis, but, as a rule, the vegetations are smaller and firmer, and there is much less tendency to ulceration. Not rarely the vegetations, too, are of a peculiar yellowish or greenish color. Involvement of the chordæ tendinæ and of the mural endocardium is also more common than in the acute cases. Embolism is of frequent occurrence.

**Symptoms.**—The onset in usually insidious, the patient complaining of increasing lassitude, anorexia, vague pains, chilly sensations, feverishness and, less often, of cardiac disturbances. For a time a suspicion of typhoid fever, influenza, tuberculosis or even neurasthenia may be entertained. Fever is, as a rule, slight at first and moderately high and irregularly remittent or intermittent in the later stages. Periods of apyrexia, lasting from a few days to two or three weeks, are not uncommon. Sweating with an occasional chill often accompanies the fever. Symptoms of cardiac involvement, such as palpitation, discomfort in the precordial region, dyspnea, cough, etc., vary considerably in degree, but in many cases they are not pronounced until late in the disease. On auscultation of the heart, however, a murmur can almost invariably be detected, most frequently in the mitral or aortic area. Petechiæ appear in the skin or conjunctival or buccal mucous membrane sooner or later in more than three-fourths of the cases. They may be abundant or so few as to be found only by careful search. Painful erythematous nodules, lasting from a few hours to three or four days, sometimes appear on the fingers, toes, hands, feet, or arms. Purpuric patches may also occur. Signs of embolism in the brain, lungs, spleen, kidneys, intestine, or larger arteries of the extremities (see p. 673) are not rarely a conspicuous feature. Embolic occlusion of large vessels was observed in 7 of 55 cases analyzed by Cotton.[1] Pain and tenderness in various joints or bones are common, and as the case progresses there is an increasing degree of weakness, loss of flesh and anemia. Although the organisms responsible for the disease are known as non-hemolytic streptococci, anemia is often profound. The leucocyte count is variable; it may be normal, subnormal or comparatively high. The infecting bacteria can be found in the circulating blood in a large

[1] Brit. Med. Jour., Dec. 4, 1920.

proportion of cases, although in the later stages they may be absent for a time. Such bacteria-free periods Libman[1] regards as evidence of partial or temporary healing. The spleen is frequently palpable and occasionally it is so large and the blood deterioration is so pronounced that the picture resembles that of splenic anemia. The skin often acquires a peculiar yellowish-white color in the course of the disease, and in the later stages, especially in bacteria-free periods, a distinctly brownish pigmentation may develop. Gastro-intestinal disturbances, the result of congestion or infarction of the abdominal organs, are sometimes an important feature. It is common to find a small amount of albumin, a few casts, and traces of blood in the urine, and occasionally there are indications of a true glomerulonephritis. With infarction of the larger renal vessels there may be pain in the back, gross hematuria and vesical symptoms. The spleen was readily palpable in 48 of Cotton's[2] 55 cases.

Subacute streptococcus endocarditis is almost uniformly fatal, although rarely it does eventuate in recovery. The usual duration is from a few months to two years. Occasionally death ensues within two or three weeks. The cause of death may be exhaustion, cerebral or pulmonary infarction, renal insufficiency or some intercurrent disease, especially pneumonia.

**Diagnosis.**—The diagnosis is often difficult, but persistent fever occurring in association with signs of valvular disease, unless it can be definitely assigned to some other cause, should always excite suspicion. If in addition to the fever, there are chills, sweats and increasing anemia, and petechiæ also occur the evidence may be considered fairly complete. In doubtful cases blood cultures are often helpful, for the finding of an anhemolytic streptococcus in the blood in the absence of any active primary focus of infection points strongly to subacute malignant endocarditis.

**Treatment.**—Any primary focus of infection which may have been concerned in producing the endocarditis should be removed, if possible. Autogenous vaccines are not likely to prove of value, although some writers have reported favorably upon their use. The general treatment is that of acute myocarditis (see p. 644).

## CHRONIC VALVULAR DISEASE

**Etiology.**—The term chronic valvular disease is applied to all chronic conditions of the cusps of the cardiac valves or of the tissues adjacent to them, which give rise to narrowing or *stenosis* of the orifices, with obstruction to the flow of blood or to *incompetence* or *insufficiency* of the valves with regurgitation of blood. The lesions are brought about in various ways, and sometimes more than one cause is operative. In more than one-third of all cases and in at least three-fourth of the cases occurring in children and adolescents the changes are traceable to *antecedent acute endocarditis*, the result of rheumatism, chorea, tonsillitis, or some other acute infection. Not rarely a *local focus of septic infection* in the tonsils, gall-bladder, Fallopian tubes, or elsewhere gives rise to recurring attacks of acute simple endocarditis, which ultimately result in permanent structural changes in the valves. *Syphilis* is an important factor, especially in the fourth and fifth decades of life. It most frequently produces aortic valvular disease, par-

[1] Trans. Assoc. American Phys., 1912, 1913; Med. Clinics of North America, July, 1918.

[2] *Loc. cit.*

ticularly aortic insufficiency, the defects being due to the extension of a syphilitic aortitis to the cusps, or to the direct implantation of the spirochæta in the cusps themselves. Relative incompetence of the mitral or tricuspid valve is often due to *chronic myocardial disease*, the valve cusps, although normal in themselves, being unable to approximate owing to relaxation of the muscular tissue and distention of the orifice. *Arteriosclerosis* is a frequent concomitant. Sometimes it is the primary lesion and produces relative mitral or tricuspid insufficiency by impairing the nutrition of the myocardium. In other cases, however, the changes in the arteries and the valves develop simultaneously, but independently, as a result of the same cause, such as gout, syphilis, muscular overwork, etc. *Chronic nephritis* is also present in many of the cases occurring in middle aged persons. It may be due to the same cause as the valvular disease or it may be the primary lesion, and by increasing the pressure within the arteries or by setting up changes in the arteries themselves it may weaken the myocardium and thus cause dilatation of an auriculo-ventricular orifice and incompetence of the valve. In a small proportion of cases valvular defects are *congenital*, being produced during intra-uterine life by an arrest of growth or by fetal disease. Pulmonary stenosis seems to be the most frequent congenital lesion. Valves that are congenitally defective are especially prone to sclerosis. Finally, in rare instances one of the valves, usually the aortic, is ruptured as the result of *sudden physical strain* or *trauma*. Such an accident is very unlikely to occur, however, in the absence of pre-existing disease of the segments.

**Morbid Anatomy.**—The lesions are of various kinds. In slight degrees of sclerosis the valve cusps are opaque, more or less thickened, and the seat of small nodular projections, which tend to prevent accurate closure of the valve. In other cases, as the result of the cicatricial contraction of much newly formed fibrous tissue, the cusps are greatly thickened, indurated and puckered or curled, the effect upon the valve being insufficiency, stenosis, or both. Shortening and thickening of the chordæ tendinæ and tips of the papillary muscles may also occur and still further impair the efficiency of the valve. Frequently as life advances, degenerative and necrotic changes supervene and bring about even greater deformity; for the devitalized areas either become calcified and transformed into hard brittle plates or they slowly disintegrate and leave behind shallow excavations, known as atheromatous ulcers. Upon the latter thrombotic deposits may collect and in turn undergo calcification. Occasionally such calcareous collections are so large that they obstruct the orifice or prevent closure of the valve. With the acute exacerbations that occur from time to time the valve segments may become welded together or adherent to the wall of the ventricle or a great vessel. In the case of the mitral valve, the segments may be uniformly united, thus producing a rigid funnel with a narrow slit at its bottom. Sclerotic valves are very prone to infection and when this occurs they present the characteristic lesions of acute simple or of acute or subacute malignant endocarditis.

**Associated Conditions.**—Changes in the myocardium are probably present to a greater or less extent in every case of chronic valvular disease. They often develop coincidently with the latter as a result one and the same cause; they may be the result of coronary sclerosis that has arisen at a later period than valvular disease and from a different cause; they may be due, at least in part, to circulatory disturbances that have been brought about directly by the valvular disease itself. General arteriosclerosis often occurs in association with valvular disease, especially in persons of middle age or older, and the same is true also of chronic nephritis. Arteriosclerosis is in some cases the cause of the valvular lesion; usually, however, it develops at

a later period as an independent condition. Occasionally valvular disease is the cause of degenerative changes in the vessels; thus, in aortic insufficiency the aorta, as a result of the extraordinary stresses to which it is subjected, may become atheromatous, and ultimately the lesions may extend to the mouths of the coronary arteries. The relations of chronic nephritis to heart disease are considered on p. 647.

Adhesive pericarditis is another frequent concomitant of chronic valvular disease, especially in children. Adhesions within the pericardium or between the latter and the chest wall or mediastinal structures add considerably to the embarrassment of the heart and thus favor the early occurrence of cardiac failure.

**Pathological Physiology.**—The tendency of chronic valvular disease is to disturb more or less seriously the equilibrium of the circulation, but owing to the extraordinary capacity of the heart to adjust itself to altered mechanical conditions, pronounced defects may exist without causing the least discomfort to the patient or impairing in any way his usefulness. This readjustment, or, as it is usually termed, *compensation*, is brought about chiefly by partial enlargements of the heart. The enlargement, which is a simple hypertrophy or, more frequently, a hypertrophy with dilatation, involves first the chamber of the heart immediately back of the valve or orifice affected, but ultimately it often extends to the entire organ. Thus, in aortic insufficiency the left ventricle, owing to the large amount of blood which it receives during diastole, first dilates, and then, owing to the increased effort required to expel the abnormally large volume of blood into the aorta during systole, it undergoes hypertrophy. Under favorable conditions these changes in the heart are so evenly balanced that notwithstanding the backflow of blood from the aorta the vessels are kept normally filled and the patient suffers no noteworthy ill effects.

The quality of the myocardial tissue determines the capacity of the heart to undergo compensatory hypertrophy and to maintain it; hence, *the outcome in any case of chronic valvular disease depends much more upon the extent and severity of the associated myocardial lesions than upon the character or degree of the valvular defect itself.* In the thoroughly degenerate heart no compensation can take place. During the period of compensation the valvular lesion is revealed only by physical signs, or, if the reserve power of the heart is reduced, by some limitation of the field of cardiac response to unusual effort. If the muscle of the heart is intrinsically good compensation once established may be well maintained for an indefinite period. In mitral insufficiency, especially, patients not infrequently live without discomfort to a ripe old age.

With weakening of the myocardium from any cause the heart becomes unable to maintain the equilibrium of the circulation, an increasing amount of blood remains in the cavities at the end of each systole, dilatation gains the ascendency over hypertrophy, the veins become surcharged with blood and the arteries correspondingly depleted, and passive congestion of the various organs ensues with the occurrence of dyspnea, cough, digestive disturbances, oliguria, etc. (see p. 747). If these symptoms occur only when unusual demands are made upon the heart and disappear quickly when the stress is removed, compensation is said to be *impaired;* but if they persist when the body is at rest, even though it has required some unusual demand to call them forth, compensation is said to be *lost.*

Failure of compensation may develop suddenly or gradually, and may be temporary or permanent. Not rarely the symptoms progress from bad to worse and eventually death occurs; but in many cases partial or complete

recovery ensues, and it is only after a series of relapses at varying intervals that the efficiency of the heart becomes permanently impaired.

There are various ways in which failure of compensation may be brought about. Immoderate physical exertion, prolonged mental or emotional strain, and intercurrent diseases often make such extortionate demands upon the heart that its reserve capacity is exhausted. In women with valvular disease symptoms of cardiac insufficiency sometimes develop during the latter part of pregnancy or shortly after parturition and are to be ascribed to the increased abdominal pressure, interference with diaphragmatic breathing, splanchnic congestion, labor pains, or sudden engorgement of the right chambers of the heart by the evacuation of the uterus. The risk is greatest in mitral stenosis and increases with succeeding pregnancies. It is especially grave when compensation has been but barely maintained prior to conception. Child-birth rarely proves harmful in mitral insufficiency when compensation is well established and the reserve force of the heart is considerable. Not infrequently other extra-cardiac conditions, such as chronic nephritis with ever increasing resistance in the peripheral vessels, arteriosclerosis with involvement of the coronary arteries or of their mouths in the aorta, anemia with progressive deterioration of the blood, etc., gradually weaken the muscle of the heart until dilatation gains the ascendency over hypertrophy. Again, the valvular lesion itself may eventually increase the work of the heart to such an extent that hypertrophy fails. In some cases, despite the presence of a marked valvular defect, the equilibrium of the circulation is well maintained until the degenerative changes incident to old age have reached an advanced stage in the arteries and heart. Sclerosis of the coronary arteries is, of course, especially important in interfering with the nutrition of the cardiac muscle.

**General Symptoms of Chronic Valvular Disease.**—When compensation is well established and the heart has still a wide margin of reserve force, disability may be trivial or absent even after severe exertion. On the other hand, when the margin of the heart's reserve force is small, the ability of the organ to respond to effort is readily exceeded and even moderate exertion may cause breathlessness, palpitation, discomfort in the cardiac region, and fatigue.

Actual rupture of compensation is attended by multifarious symptoms, the result of passive congestion of the organs and of deranged digestion, absorption, excretion and metabolism. Dyspnea, more or less severe, is always present. It arises from various causes, the chief of which are congestion of the lungs, pulmonary edema, and compresson of the lungs by hydrothorax. In cases associated with severe renal lesions acidosis may also be a factor. Sometimes the dyspnea assumes a paroxysmal character, as in asthma, the attacks being usually at night (see p. 605). Toward the end, when cardiac failure is marked, breathing of the Cheyne-Stokes type may be observed. Accompanying the dyspnea there is often cough with more or less mucoid or muco-purulent expectoration. In mitral lesions, especially mitral stenosis, bloody expectoration or even hemoptysis may occur as a result of the extreme engorgement of the lungs or of pulmonary infarcts.

Passive congestion of the alimentary canal may give rise to anorexia, flatulence, pyrosis, vomiting and irregular action of the bowels; of the liver, to uniform enlargement of the organ, with tenderness, a sense of discomfort or actual pain in the right hypochondrium, and perhaps slight jaundice; and of the kidneys, to oliguria with concentration of the urine, albuminuria and even slight hematuria.

With increasing engorgement of the general venous system edema

develops. It usually begins first in the subcutaneous tissues about the ankles and gradually ascends. For a time it may be present only during the day, when the patient is about, rest in the recumbent position causing it to disappear. Later, it may become more or less general and involve the serous sacs, ascites, hydrothorax, and hydropericardium occurring successively or coincidently. In some cases, hydrothorax, especially of the right side, appears first and outlasts other edematous infiltrations (see p. 628).

Subjective symptoms referable to the heart are frequently present. These usually consist of palpitation and a sense of oppression on exertion. Severe pain is not common, except in aortic insufficiency, in which lesion there may be paroxyms of true angina pectoris. In mitral disease, especially stenosis, slight lancinating pains with circumscribed tenderness often occur in the region of the apex.

When the valvular defect is considerable, varying degrees of cyanosis are frequently observed; indeed, in mitral lesions blueness of the lips, ears and hands, with capillary injection of the cheeks, may be for a long time the only evidence of circulatory embarrassment and in certain congenital defects of the valves lividity is the most striking feature. Sometimes, and especially in aortic lesions, there is marked pallor instead of cyanosis.

Nervous symptoms, such as headache, vertigo, syncopal attacks, and disturbed sleep with distressing dreams, are somewhat frequent, particularly in defects of the aortic valve, and are usually to be ascribed to disturbances of the cerebral circulation. However, the mere knowledge that a valvular lesion exists may be sufficient to excite various nervous phenomena in persons of an impressionable temperament. Occasionally a true psychosis supervenes. It may take the form of mental confusion with disorientation, of hallucinations of sound or vision, of definite delusions, or even of an actual mania. As Riesman[1] points out in discussing the subject, cardiogenic psychoses may be the results of drugs, especially digitalis, of renal insufficiency, of acidosis, of a preëxisting psychopathic taint, or of some direct disturbance of the cerebral circulation. Just before death in heart disease the patient may become delirious, then stuporous and finally comatose as a result of acidosis, uremia, or extreme exhaustion.

**Physical Signs.**—Objectively, chronic valvular disease is usually made evident by adventitious sounds, known as murmurs or bruits, and by signs of enlargement of the heart. Palpable vibrations, or thrills, abnormal pulsations and certain peculiarities of the pulse are other manifestations that may also be present.

*Murmurs.*—A murmur the result of valvular disease is produced either by obstruction to the onward flow of blood, as when an orifice is narrowed or roughened (stenosis) or by a leakage of blood backward, as when a valve is no longer competent (insufficiency). Neither the character nor the intensity of a murmur conveys any information as to the nature of the valvular lesion or the extent of the structural change, although these attributes may aid in distinguishing one murmur from another when two or more are present. On the other hand, the point of maximum intensity of a murmur, the direction in which it is most distinctly conducted, and the time of its occurrence in the cardiac cycle are points of great value in determining which particular valve is affected and whether the functional derangement is stenosis or insufficiency.

As a rule, a murmur is heard best at a point on the surface of the chest which is nearest to the valve at which the murmur is produced. Thus, a murmur produced at the aortic orifice is usually heard with maximum intensity where the aorta becomes most superficial, that is in the second right

[1] Amer. Jour. Med. Sci., Feb., 1921.

intercostal space, or owing to contact of the aorta with the manubrium sterni, which is an excellent conductor of sound, over that bone or just to the left of it; while a murmur produced at the mitral orifice is usually heard loudest where the left ventricle becomes most superficial, which is at or just above the apex.

In general, a murmur is transmitted in the direction in which the blood is flowing at the time of its production, although the conducting power of the tissues interposed between the heart valves and the chest-wall also exerts some influence upon its propagation. Thus, the murmur of aortic insufficiency has a tendency to be transmitted toward the apex of the left ventricle, but owing to the good conducting properties of the overlying sternum it may be conveyed more distinctly to the ensiform cartilage. Murmurs may occur at any period of the cardiac cycle. A systolic murmur is one occupying the whole or a part of the period from the beginning of the first to that of the second sound, and a diastolic murmur is one occupying a whole or a part of the period from the beginning of second sound to that of the first. A murmur occurring at the end of ventricular diastole (auricular systole) or just before ventricular systole is referred to as a presystolic murmur. Systolic murmurs at the aortic or pulmonary orifices are signs of obstruction, while at the auriculo-ventricular orifices they are signs of insufficiency or regurgitation. Presystolic murmurs are rarely produced elsewhere than at the auriculo-ventricular orifices and signify obstruction. It must be borne in mind, however, that the mere presence of a murmur does not in itself justify the diagnosis of organic valvular disease. Systolic murmurs at the base of the heart are much more frequently due to anemia, aneurysmal dilatation of the aorta, or simple roughening of the aortic leaflets than to the aortic stenosis, and systolic murmurs at the apex are often the result of unimportant functional derangements. Diastolic and well-marked presystolic murmurs, on the other hand, usually signify true valvular defects.

*Enlargement of the heart* in chronic valvular disease is caused by compensatory hypertrophy or dilatation. It is detected by percussion and even more accurately, perhaps, by the *x*-ray. Enlargement of the left side of the heart increases the area of cardiac dulness chiefly in the vertical direction, while enlargement of the right side of the heart increases the area of dulness transversely. The impulse is usually diffuse and, if hypertrophy is ascendant, "heaving" or if dilatation is ascendant, weak and tapping. The apex beat is displaced downward and to the left, the downward displacement being especially marked in enlargement of the left ventricle.

A *thrill* is a vibrating sensation felt on palpation especially in the region of the heart. It is not peculiar to valvular disease, but may be observed also in aneurysm of the aorta and patent ductus arteriosus. It may be systolic, presystolic, or diastolic. Systolic thrills at the base indicate aortic aneurysm, stenosis of the aortic orifice or roughening of the aortic valve, or, rarely, pulmonary stenosis. Systolic thrills are uncommon at the apex, but they may occur in mitral insufficiency. An apical presystolic or diastolic thrill is strongly indicative of mitral stenosis and sometimes may be felt when no murmur can be heard.

*Abnormal Pulsations.*—Exaggerated pulsation of the carotid arteries is often observed in aortic insufficiency, but other conditions, such as exophthalmic goiter, carotid aneurysm and anemia may also cause it. In many healthy persons pulsation (alternate filling and collapse) in the jugular veins may be seen just above the clavicle, especially when the individual is recumbent. This pulsation occurs twice as frequently as that seen in the carotid artery, and in contrast with the latter is diffuse, wavy, and rarely palpable.

Further, it consists of two waves, one being synchronous with the auricular systole, the other occurring at the end of the ventricular systole. The term "physiologic," "negative" or "double" is applied to it. Marked distention or pulsation of the jugulars is observed in overfilling of the right auricle from various causes, such as valvular disease, lesions of the lungs which impede the pulmonary circulation, and compression of the superior vena cava by mediastinal tumors, etc.

In auricular fibrillation or even extreme distention of the right auricle and insufficiency of the tricuspid valve, the physiologic or double venous pulse is replaced by one wave which is synchronous with the ventricular systole. This abnormal venous pulsation is known as the "positive," "ventricular" or "single" form of venous pulse. It is caused by the forcing backward of the blood during ventricular systole into the auricle and from there into the veins. If the vein be emptied by stroking it from below upward, and its upper extremity be kept closed it instantly refills from below and continues to pulsate.

Visible or palpable epigastric pulsation is frequently noted in hypertrophy of the right ventricle, but it may occur also in other conditions, such as displacement of the heart to the right, aneurysm of the abdominal aorta, tumors resting upon the abnormal aorta, and depression of the diaphragm from emphysema or visceroptosis.

Pulsation of the capillaries is a common, but by no means a constant, sign in aortic insufficiency. It is best appreciated by observing the alternate blushing and blanching under the finger nail, especially when the free margin of the latter is slightly compressed, or in the mucous membrane of the lower lip when a glass slide is pressed lightly upon its surface. Conditions with low diastolic pressure, other than aortic insufficiency, such as anemia and exophthalmic goiter, also occasionally produce a capillary pulse.

*The Pulse.*—Aortic insufficiency and aortic stenosis are the only forms of valvular disease with a distinctive pulse. In aortic insufficiency the pulse wave is very large, with a quick upstroke and a sudden fall, making the artery appear empty between the beats (water-hammer or Corrigan pulse). These characteristics are best perceived when the arm is raised above the head and the wrist is grasped in the whole hand. In typical cases of aortic stenosis the pulse is infrequent (pulsus rarus), small (pulsus parvus) and slow to rise and slow to fall (pulsus tardus).

Arhythmia is common in all forms of valvular disease, but it is the result of coincident lesions in the myocardium rather than of the valvular defects. The blood pressure is variable. Even when there is pronounced myocardial insufficiency, however, it may be normal or above normal.

**Complications.**—Overdistention of the pulmonary and systemic veins favors the occurrence of *chronic bronchitis*, *gastritis*, *enteritis*, *nephritis*, etc. Long-continued stasis of blood in the hepatic veins may lead to *cyanotic induration of the liver*. *Edema of the lungs* is a frequent cause of death. Sclerotic valves are much more susceptible to infection than healthy ones and in consequence *acute endocarditis*, simple or malignant, often supervenes. The frequent association of *myocarditis*, *pericarditis*, and *arteriosclerosis* has already been mentioned.

The unnatural eddying of the blood and the retardation of the current favor the formation of *thrombi*. These are usually intracardiac, the appendices of the auricle and the auricle itself being the most common sites. Thrombosis of the peripheral veins as a result of chronic valvular disease is rare. Welch[1] in 1900 collected from the literature 27 cases. In 23 cases

[1] Phila. Medical Jour., May 5, 1900.

the thrombi were in the veins of upper extremities or the neck, or both, and in only 4 were the veins of the lower extremities involved. In the majority of cases the valvular lesion was mitral stenosis.

*Embolism* is not an uncommon complication, especially in mitral disease. It was observed in 85 of 250 cases of heart disease examined post-mortem by Ginsburg.[1] The embolus may be derived from a vegetation that has been formed on one of the valves in a recurrent attack of endocarditis or from a thrombus that has been deposited between the muscular trabeculæ in one of the chambers of the heart. The emboli usually lodge in one of the small arteries of the lungs, spleen, kidneys or brain. More rarely a peripheral artery, the superior mesenteric artery, retinal artery, celiac axis, or abdominal aorta is occluded.

## MITRAL INSUFFICIENCY

Mitral insufficiency is the commonest form of chronic valvular disease. It may be due (1) to curling and retraction of the valve-leaflets or distortion of the musculi papillares or chordæ tendinæ, as a result of a previous attack of acute endocarditis or of a primary degenerative process; or (2) to distention of the mitral orifice in consequence of relaxation of the surrounding muscular tissue or dilatation of the left ventricle (relative insufficiency). The lesions resulting from acute endocarditis are often of such a character that they cause not only insufficiency, but some degree of stenosis as well. Relative mitral insufficiency may be a sequel of aortic insufficiency or stenosis or of persistent high blood pressure, or it may be the result of primary myocardial insufficiency.

**Effects.**—The changes in the heart resulting from mitral insufficiency involve the left auricle, left ventricle, and right ventricle. The left auricle becomes dilated and then undergoes hypertrophy, owing to the extra amount of blood that is discharged into it in each ventricular systole. The left ventricle is similarly affected in consequence of the increased volume of blood driven into it from the auricle in each diastole. The overdistention of the left auricle increases the tension in the pulmonary veins and this in turn leads to hypertrophy and dilatation of the right ventricle. Ultimately there may be stretching of the tricuspid orifice, relative tricuspid insufficiency and enlargement of the right auricle. In typical cases the heart is enlarged transversely and the apex is rounded.

So long as the left auricle and right ventricle are capable of handling the excess of blood and the left ventricle is able to discharge into the aorta, notwithstanding the leakage at the mitral valve, the normal volume of blood, the patient experiences no noteworthy discomfort. Compensation may thus be maintained for an indefinite period. However, when the left auricle, owing to muscular insufficiency or to excessive regurgitation, is no longer able to empty itself completely engorgement of the pulmonary vessels ensues, and later when the right ventricle becomes so strained and distended that the tricuspid valve is rendered incompetent, congestion of the whole venous system occurs.

**Special Symptoms.**—The earliest symptoms of failing compensation are usually referred to the lungs and consist of dyspnea, cough, and perhaps cyanosis. In consequence of stasis there is a pronounced tendency to bronchial catarrh. For the same reason attacks of hemoptysis may also occur, although they are less common than in mitral stenosis. Symptoms of indigestion often appear early. Although palpitation and a sense of oppression in

[1] Arch. f. klin. Med., Bd. lxix, Heft 5 u. 6.

the region of the heart are frequently present, typical angina pectoris is rare. With dilatation of the right ventricle and occurrence of tricuspid insufficiency, edema and the symptoms of visceral stasis, which have already been considered, supervene.

Unless there is also extensive degeneration of the myocardium, the fatal termination is rarely sudden. In the majority of cases the end comes after repeated attacks of disturbed or broken compensation, through increasing cardiac asthenia or pulmonary edema. Not rarely death results from some intercurrent disease, such as pneumonia or nephritis, or from embolism.

**Physical Signs.**—*Slight bulging of the precordium is sometimes observed, especially in children. The apex beat is displaced to the left and not rarely somewhat downward. The area of cardiac dulness is increased both to the left and to the right. A systolic murmur is heard loudest at or just above the apex beat and is transmitted to the axilla and frequently to the angle of the left scapula. The second pulmonic sound is usually accentuated and may be reduplicated.*

In adults, owing to the rigidity of the thorax, bulging of the precordium is not often observed. In addition to the apex beat a pulsation is sometimes seen in the second or third left intercostal space (conus arteriosus) and in the epigastrium (enlarged right ventricle). In some cases there is a diffuse pulsation over the entire precordium. A thrill at the apex is occasionally noted.

When the degree of insufficiency is slight the enlargement is usually inconsiderable. In the later stages of severe cases, however, the dulness may extend upward to the second rib, to the left as far as the anterior axillary line, and to the right as far as the right parasternal line. The murmur replaces or accompanies the first sound. It is of variable length and quality. Usually it is soft and blowing, but it may be harsh or even musical. No importance is to be attached either to the character or to the intensity of the murmur in estimating the degree of insufficiency. A loud harsh murmur often implies forcible ventricular contractions and a feeble whiff the reverse. On the other hand, the murmur of relative insufficiency may entirely disappear with restoration of the normal tone of the cardiac muscle. In many cases the murmur is louder when the patient is recumbent than when he is erect, and occasionally it is heard only when he is recumbent.

The accentuation of the second pulmonic sound is an indication of increased tension in the pulmonary artery and of a forcibly contracting right ventricle. It usually disappears when compensation is broken.

In well compensated cases the pulse is usually full and regular and of normal or slightly subnormal tension. In the later stages of the more severe forms of the disease pronounced irregularity, usually the result of auricular fibrillation, often develops.

**Diagnosis.**—The mere presence of a systolic murmur at the apex is not of itself evidence of either shortening of the mitral cusps or of weakness of the myocardium and relaxation of the mitral ring. Such murmurs are frequently abnormal breath sounds produced by the movements of the heart upon the adjacent lung tissue (cardio-respiratory murmurs) or accidental sounds of obscure origin and of no pathologic significance. It may be assumed that an apical systolic murmur is functional, or at least innocent, if the heart is not enlarged, the second pulmonic sound is not accentuated, the pulse rate is normal, the blood pressure is normal, and the individual's response to exercise is good. *Cardiopulmonary murmurs* are common and as a rule, readily recognized. They usually disappear during recumbency and often when the breath is held, and are greatly influenced by respiration, being heard best at the height of deep inspiration and expiration and suddenly

disappearing at the end of each act. *Hemic murmurs* are usually heard loudest over the pulmonary area, but sometimes they are heard best at the apex. They are nearly always soft and blowing; they vary considerably with the phases of respiration and with change of position; they are frequently accompanied by a continuous hum in the veins of the neck ("bruit du diable"); and they are associated with the usual evidences of anemia.

When *tricuspid insufficiency* coexists with mitral insufficiency, the diagnosis of the former may be difficult. The existence of two areas of pronounced audibility, one near the xiphoid cartilage, the other at the apex, the recognition of a difference in the quality or pitch of the murmurs in these two areas, and the occurrence of a systolic jugular pulse and of enlargement of the liver with systolic pulsation are the only criteria by which an exact diagnosis of tricuspid insufficiency can be made.

It is not always possible to distinguish between *organic* mitral insufficiency and *relative* mitral insufficiency. The previous history of the case should be carefully considered. A history of rheumatism or of some other infection likely to cause endocarditis, the coexistence of a presystolic or diastolic murmur (evidence of associated mitral stenosis), the presence of a thrill, accentuation of the pulmonary second sound, and propagation of the systolic murmur beyond the mid-axillary line point definitely to organic disease. The large majority of cases of mitral insufficiency developing after the fortieth year in persons who give no history of acute rheumatism are due to stretching of the mitral ring.

## MITRAL STENOSIS

Mitral stenosis results from thickening and welding together of the valve leaflets or from cicatrization and contraction of the tissues surrounding the orifice. It is usually associated with mitral insufficiency, of which it is sometimes a sequel. All degrees of obstruction are encountered. Not rarely, especially in children, the valve is transformed into a hollow membranous cone with a small aperature at its apex—the funnel-shaped form of mitral stenosis. In other cases, chiefly in adults, fusion of the segments and contraction of the surrounding tissues reduce the orifice to a narrow slit—the buttonhole form of mitral stenosis.

**Etiology.**—As rheumatism, chorea, and tonsillitis are the chief etiologic factors, the disease is especially common in early life. In adults it occasionally develops as the result of a degenerative process analogous to arteriosclerosis. In some cases no etiologic factor can be determined with certainty. Females are more frequently affected than males. Of 53 cases studied postmortem by Broadbent, 38 were in females, and of 60 cases studied clinically by Steell, 41 were in females.

**Effects.**—The secondary changes in the heart involve chiefly the left auricle and the right ventricle. In consequence of the hindrance to the outflow of blood the left auricle becomes hypertrophied and then dilated. The appendix of the auricle is especially affected, sometimes becoming enormously distended and elongated. The increased tension in the pulmonary veins leads to hypertrophy and eventually to dilatation of the right ventricle. When the latter becomes pronounced tricuspid insufficiency ensues with the occurrence of general venous congestion. In pure mitral stenosis the left ventricle is rarely enlarged; indeed, owing to imperfect distention of its cavity during diastole it tends to become somewhat smaller.

According to Samways,[1] of 196 cases of mitral stenosis that came to

[1] Brit. Med. Jour., Feb. 5, 1898.

autopsy tricuspid stenosis was also present in 32 and pericarditis in about one-third of the number. As a result of the slowing of the blood stream and changes in the endocardium, antemortem thrombi are frequently formed in the auricular appendix or in the auricle itself. Sometimes these thrombi are attached by slender pedicles like polypi and in rare instances they are entirely free and of a globular shape.

**Special Symptoms.**—As a rule, compensation is not maintained so long in mitral stenosis as in mitral insufficiency; nevertheless the patient often enjoys robust health for many years. In young children the disease is not rarely associated with imperfect physical development and faulty nutrition. As in mitral insufficiency the earliest symptoms are usually referable to the lungs and consist of dyspnea, cough and cyanosis on exertion. Bronchial catarrh is a common and often a troublesome complication. In consequence of the high pressure in the pulmonary veins or of actual infarcts in the lung, hemoptysis frequently occurs. Indeed, the symptoms may resemble those of pulmonary tuberculosis. A tendency to epistaxis is also marked in many cases. Hoarseness from compression of the left recurrent laryngeal nerve against the aorta by the enlarged left auricle, either directly or through the interposition of the pulmonary artery, is occasionally observed. Garland and White[1] add 9 cases of paralysis of the left recurrent laryngeal nerve with mitral stenosis to 61 others from medical literature.

Palpitation and darting pains over the heart, especially in the region of the apex, are present in a large proportion of cases, but true angina pectoris is rare. It was noted but once in connection with mitral stenosis in 1500 cases of valvular disease studied by Nothnagel. An area of tenderness is frequently found in the region of the apex.

With failure of compensation the increased tension in the inferior vena cava eventually leads to engorgement of the abdominal organs and to edema of the legs. This last symptom, however, appears later, as a rule, than in mitral insufficiency, and many cases of stenosis run their entire course without it. The liver is often considerably enlarged, and, from the stretching of its capsule, the seat of pain and tenderness. Menorrhagia is a common symptom, and copious flooding is likely to occur in labor.

Embolism occurs more frequently in mitral stenosis than in any other form of chronic valvular disease. In the majority of cases the emboli are fragments of thrombi which have been deposited in the recesses between the trabeculæ, but occasionally they are detached masses of vegetations, which have been formed during an attack of recurring endocarditis.

Death in mitral stenosis is usually preceded by a period of increasing cardiac embarrassment, which is terminated more or less abruptly by some pulmonary complication such as edema, infarction or pneumonia. Sudden unexpected death is rare.

**Physical Signs.**—The most characteristic physical signs of mitral stenosis are: *a presystolic thrill at the apex ending in a sudden, sharp, tapping apex beat; enlargement of the area of cardiac dulness transversely, especially to the right; a low-pitched, rumbling murmur, audible over a very limited area at the apex or a little to the right or left of the apex, and either mid-diastolic in time or definitely presystolic with a loud, snappy first sound; and accentuation of the second sound in the pulmonic area.*

Bulging of the precordium is sometimes seen in children. The displacement of the apex beat to the left is not usually so pronounced as in mitral insufficiency. In addition to the apex-beat, there may be pulsation in the epigastrium and also in the third left interspace near the sternum (enlarged conus

[1] Archiv. Inter. Med., Sept. 15, 1920.

arteriosus). The tactile thrill is present in the large majority of cases. It begins in the diastole, gathers strength as it progresses, and often ends abruptly in the sudden sharp shock of the first sound. In some instances the thrill is appreciable only after exertion or when the patient is in a certain posture. Occasionally it may be felt even when no murmur can be heard.

The area of cardiac dulness is not often increased much to the left unless there is a considerable degree of incompetence with the stenosis. In pronounced obstruction, however, the dulness not rarely extends higher than normal, owing to dilatation of the conus arteriosus. The murmur is usually heard best a little to the left or right of the apex beat, and, is, as a rule, very limited in its dissemination, the area of audibility often not exceeding 3 or 4 centimeters in diameter. In some cases the murmur can be heard only after exercise and when the patient is recumbent and with body inclined toward the left side. The typical murmur is one of a rumbling vibratory character. It often begins an appreciable time after the second sound and increases in intensity in a crescendo manner until it terminates abruptly in the first sound, which is characteristically sharp and snappy. In many cases, however, probably the majority, the murmur lacks the presystolic accentuation and is definitely mid-diastolic in time and diminuendo in character or it occupies virtually the whole of diastole and is accentuated at the beginning and at the end of the period. With the occurrence of auricular fibrillation the murmur, if previously presystolic, becomes mid-diastolic or early diastolic, and usually soft and blowing instead of rumbling. Occasionally it disappears while fibrillation persists. Even in the absence of fibrillation or of pronounced cardiac weakness the murmur of mitral stenosis shows a tendency to disappear from time to time in the most erratic way, leaving only the loud, snappy first sound which in itself is almost characteristic. So long as compensation is well maintained the second pulmonic sound is usually accentuated and may be palpable. In some instances it is also reduplicated.

Occasionally, instead of accentuation of the second pulmonic sound, a soft, blowing diastolic murmur, resembling that of aortic insufficiency, may be heard to the left of the sternum, about the third intercostal space. This murmur, which is known as the Graham Steell murmur, is probably due to relative insufficiency of the pulmonic valves, from dilatation of the right ventricle. Not rarely a third loud heart sound is audible in the fourth interspace near the sternum. It is thought to be due to the sudden tension on the edges of the mitral valve when it attempts to open widely but cannot. The electrocardiogram in mitral stenosis usually shows marked right ventricular preponderance and a prominent auricular (P) wave. The pulse is in no way characteristic. Auricular fibrillation, however, occurs more frequently than with other valvular lesions and when this condition supervenes the pulse becomes completely irregular.

**Diagnosis.**—The recognition of mitral stenosis is usually not difficult. Even when the murmur is absent, the diagnosis may be ventured in the presence of a tapping, systolic impulse, a short, loud, snapping first sound, and accentuation of the pulmonic second sound. However, as presystolic apical murmurs may result from causes other than mitral stenosis, the diagnosis is not uniformly easy. Phear[1] analyzed 46 cases in which a presystolic apical murmur was heard during life and no mitral lesion was found at autopsy. In 17 of these the aortic valves were incompetent, and in 20 the pericardium was adherent. In 12 instances a presystolic or diastolic thrill was also present.

The presystolic murmur which is sometimes heard at the apex in uncom-

[1] Lancet, Sept. 21, 1895.

plicated cases of aortic insufficiency (*Flint's murmur*) may occasionally be mistaken for the murmur of organic mitral stenosis. Flint's murmur, however, is rarely harsh like the latter, and is not accompanied by a sharp systolic shock, a snapping first sound, or an accentuated pulmonic second sound. Moreover, the pulse changes which are characteristic of uncomplicated aortic insufficiency are often poorly developed when true mitral stenosis is also present. Finally, in uncomplicated aortic insufficiency there is no electrocardiographic evidence of marked right ventricular hypertrophy or of auricular hypertrophy. *Adherent pericardium* does not produce the sudden tapping impulse or the characteristic first sound of mitral stenosis, and is sometimes suggested by systolic retraction anteriorly in the region of the apex and posteriorly between the eleventh and twelfth ribs. *Tricuspid stenosis* is rare. It is usually associated with mitral stenosis and is almost never found as an insolated valvular lesion. Its coexistence may be inferred only when the two murmurs vary in point of maximum intensity and quality, when cyanosis appears early and is marked, and when an auricular type of hepatic pulsation is present. A presystolic murmur may also occur in *aneurysm of the left ventricle*, and in *aneurysm of the mitral valves*, but, of course, such lesions are exceedingly rare, and the difficulties in the way of a correct diagnosis are well nigh insuperable.

A slight presystolic thrill and even a slight presystolic murmur are sometimes observed in *healthy persons in whom the chest wall is thin and the heart is irritable*, but in such cases there is no history of antecedent rheumatism or chorea, the second sound is not usually accentuated or reduplicated, the first sound rarely has the sharp and snappy character of true mitral stenosis, and no right ventricular enlargement is shown by percussion, roentgenography or electrocardiography.

## AORTIC INSUFFICIENCY

Aortic insufficiency ranks second in the order of frequency with which the individual heart valves are affected. The lesion is much more common in men than in women and occurs most frequently in the middle period of life. In the vast majority of cases it is brought about by cicatricial retraction or curling of the aortic leaflets, the result of endocarditis or a sclerotic process extending downward from the aorta. The insufficiency is often associated with some degree of stenosis. Syphilis, rheumatism and severe muscular strain are the chief etiologic factors. Occurring in young men as an isolated valvular lesion, it is usually due to syphilis. In children and adolescents it is often the result of rheumatism, and in this case the mitral valve is also usually affected. In late life aortic incompetence is not rarely caused by senile degenerative changes similar to those occurring elsewhere in the aorta and in the arteries generally. In rare instances the lesion develops suddenly, one of the valve-segments being torn during violent muscular effort, such as the exertion of lifting a heavy weight or a struggle to avoid a fall. It is doubtful, however, whether the rupture of a healthy leaflet can occur from this cause. Occasionally perfect coaptation of the valves is prevented by vegetations on their free surface, or leakage occurs from a loss of tissue due to ulcerative endocarditis. Finally, the insufficiency may be relative, the aortic ring having been stretched by an aneurysm at the origin of the aorta, by atheromatous dilatation of the aortic arch (Hodgson's disease), or possibly by pronounced cardiac dilatation.

**Effects.**—The increased intraventricular pressure resulting from the regurgitation of blood from the aorta during each diastole causes permanent

dilatation of the left ventricle, while the increased labor entailed in expelling an abnormal amount of blood during each systole leads to compensatory hypertrophy. Later sequences are stretching of the mitral ring, relative insufficiency of the mitral valve, enlargement of the left auricle and finally dilatation of the right ventricle and relative insufficiency of the tricuspid valve. The heart attains a larger bulk than in any other valvular affection, sometimes weighing 12,000 grams (40 ounces) or more (cor bovinum). The sudden expulsion of an increased amount of blood from the left ventricle tends to dilate the aorta and to produce in it degenerative changes or to intensify these if they have already existed.

**Special Symptoms.**—Aortic insufficiency, especially that form which follows acute endocarditis, is sometimes borne without discomfort for many years. Indeed, there are cases in which the heart is so well adapted to its increased work that the patient can engage in the most vigorous physical exercises without the slightest inconvenience. Nevertheless, when compensation does fail it is restored with greater difficulty than in any other form of valvular disease.

The early symptoms of aortic insufficiency are usually attributable to arterial anemia or cardiac fatigue and not, as in mitral disease, to venous stasis. Vertigo, headache, flashes of light, and tinnitus aurium are common cerebral symptoms. Sudden cerebral anemia may also occur on exertion, inducing syncope. In some cases dyspnea and palpitation are prominent features; in others, precordial pain is the chief cause of complaint. Not rarely the pain presents all the characteristics of true angina pectoris. Pallor of the face is much more common than in mitral lesions.

Late in the disease, when the mitral valve becomes incompetent, cyanosis, cough, hemoptysis, and general dropsy supervene, but in many cases death occurs before this stage is reached. The fatal termination is more likely to be sudden in aortic insufficiency than in any other form of valvular disease. This catastrophe results from angina pectoris or from syncope, usually after some effort, the left ventricle failing abruptly in diastole. In some cases the end comes more gradually through pulmonary edema, recurring endocarditis, or infarctions.

**Physical Signs.**—In typical cases there is *some bulging of the precordium; the impluse of the heart is vigorous and diffuse; the apex beat is well to the left of the mid-clavicular line and often in the sixth or seventh intercostal space; the peripheral arteries are forcibly distended at each systole and the pulse is full, quick and collapsing (water-hammer or Corrigan's pulse); the capillaries are often the seat of visible pulsations; the area of cardiac dulness is increased to the left and downward; a diastolic murmur is heard at the base of the heart and is transmitted downward to the xiphoid cartilage or toward the apex; and the pulse-pressure, owing chiefly to a low diastolic reading, is usually markedly increased.*

Owing to the great size of the left ventricle, the protrusion of the precordium and the outward and downward displacement of the apex beat are usually more pronounced than in other valvular diseases. A characteristic feature is the violent, jerky pulsation of the peripheral arteries. This may be noticeable not only in large arterial trunks, such as the carotids, brachials and femorals but also in small vessels, such as those of the hands, feet, pharynx and retina. With each systole they "are projected forcibly from their bed, and bound under the skin." Not rarely the pulsations are sufficiently strong to produce movements of the head. Occasionally, an arterial pulsation is perceptible in the liver. The pulse on palpation is also distinctive. The wave strikes the finger suddenly, distends the artery to extreme fulness and

instantly recedes leaving the vessel apparently empty. These peculiarities, first accurately described by Sir Dominic Corrigan, are made more apparent by grasping the patient's wrist in the hand and holding his arm above his head. They are due in part to the forcible discharge of an abnormal quantity of blood into the depleted arteries in systole and the prompt return of a part of this blood to the ventricle in diastole, and probably also in part to reflex dilatation of the arterioles, the result of the increase in intraventricular pressure. A sphygmographic tracing of the pulse (Fig. 29) shows an abrupt upstroke with a sudden fall and the dicrotic notch lying below the middle of the pulse wave. Frequently the interval between the apex beat and the radial pulse is considerably increased.

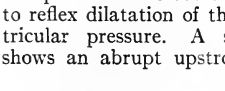

FIG. 29.—Sphygmogram from a case of severe aortic insufficiency showing the low position of the dicrotic notch.

Aortic insufficiency is the only valvular disease that characteristically affects the blood-pressure. Compared to the systolic pressure, which may be higher than normal, the diastolic pressure is very low and in consequence the pulse pressure is abnormally high. Moreover, the systolic pressure is distinctly higher in the legs than in the arms and in the distal segments of both upper and lower extremities than in the proximal segments.

The capillary pulse (see p. 682) is present in about three-fourths of the cases. It is not absolutely pathognomonic of aortic insufficiency, being occasionally observed in other conditions accompanied by pronounced relaxation of the arterioles. As a result of the greatly increased pulse pressure, pulsation is exceptionally observed in the superficial veins, especially those on the back of the hands.

The diastolic murmur of aortic insufficiency is in most cases soft and blowing; sometimes, however, it is harsh, and occasionally it is distinctly musical. With failing compensation it may become faint or inaudible. In a large proportion of cases the maximum intensity is not in the so-called aortic area, or inner end of the second right intercostal cartilage, but in the third or fourth left interspace close to the sternum, or immediately over the sternum, opposite the third costal cartilages. From the point of maximum intensity the murmur is propagated downward, usually more in the direction of the xiphoid cartilage than toward the apex, where it is often feeble or inaudible. Occasionally it can be heard in the carotids. The second sound at the base may be wholly replaced by the murmur or it may be audible as well as the murmur. The first sound at the base may be clear, but in many instances it is accompanied or replaced by a systolic murmur. The latter may be due to a true stenosis of the aortic orifice, or, which is more frequently the case, to atheromatous roughening of the aortic valves or the wall of the aorta or to dilatation of the aortic arch. In the advanced stages of the disease, the first sound at the apex also may be accompanied or replaced by a systolic murmur; this is commonly the result of relative mitral insufficiency. In some instances a presystolic murmur is audible at the apex, even when there is no coexisting mitral stenosis; this is the so-called Flint murmur, Austin Flint first having drawn attention to it in 1862. It is probably due to vibrations transmitted to the apex from the anterior leaflet of the mitral valve, the latter being impinged upon by the regurgitant current from the aorta, and also, perhaps, by the normal current from the auricle. The differention of this murmur from that of a true mitral stenosis has already been considered (see p. 688).

A loud, sharp systolic sound (pistol-shot sound) is sometimes heard over

the larger arteries, especially the femorals. It is of local origin. When the stethoscope is pressed somewhat firmly upon the femoral artery a diastolic murmur may be audible in addition to the systolic murmur (pressure murmur) thus normally produced. This diastolic murmur, which is known as Duroziez's sign, is thought to be due to a regurgitant current passing from the periphery toward the heart.

In estimating the extent of the regurgitation the most important factors to be considered are the size of the left ventricle, the degree of collapse in the radial pulse, and the height of the pulse pressure. According to Broadbent, a second sound over the carotid artery indicates that the regurgitation is not excessive and that the arterial pressure is being well maintained.

**Diagnosis.**—The diagnosis of aortic insufficiency is not often difficult. *Dilatation of the aorta*, which not rarely follows aortic insufficiency, may, however, be mistaken for *aneurysm*, as it sometimes produces pulsation and dulness in the second right interspace and is accompanied by a systolic murmur. Roentgenography will usually lead to a correct opinion.

## AORTIC STENOSIS

Although a moderate degree of narrowing of the aortic orifice is present in many cases of aortic insufficiency, uncomplicated aortic stenosis is relatively rare. Kelynack[1] found but 2 cases in 1635 necropsies and Norris[2] found only 48 cases in the necropsy records of 9940 cases having cardiac lesions. The disease occurs most frequently as a part of a general arteriosclerosis in persons past middle age. It is more common in males than in females. In young subjects is usually a sequel of rheumatic endocarditis. Occasionally, it is congenital.

**Morbid Anatomy.**—The leaflets are thickened, rigid, and often adherent. Sometimes the orifice is so constricted by the cohesion of the segments that it will scarcely admit a penholder. The tissues of the aortic ring may also be thickened and contracted. In other cases a high grade of stenosis is caused by the formation of large thrombi on the ventricular surfaces of the valves or in the sinuses of Valsalva.

The primary effect of the abnormal resistance at the aortic orifice is simple hypertrophy of the left ventricle. For a long time there may be little or no accompanying dilatation. Ultimately, however, the ventricle yields to the severe strain and in so doing occasions relative insufficiency of the mitral valve and a backing up of blood in the general venous system.

**Special Symptoms.**—The disease often remains latent for a long period, the left ventricle being sufficiently strong to maintain a normal volume of blood in the arteries notwithstanding the excessive resistance at the aortic orifice. The earliest symptoms are usually attributable to cerebral anemia and consist of vertigo, sleeplessness, and faintness on exertion. Precordial pain is not uncommon. Dyspnea, cough, edema, etc. do not appear until the mitral sphincter yields and, in consequence, the right chambers of the heart become embarrassed. Not infrequently before these symptoms supervene death occurs from angina pectoris or some intercurrent disease.

**Physical Signs.**—Typical cases present the following physical signs: *Displacement of the apex beat downward and somewhat to the left; a systolic purring thrill at the base of the heart, especially in the second right intercostal space; enlargement of the area of cardiac dulness downward and to the left; a systolic murmur with maximum intensity in the aortic area, well conducted*

[1] Med. Press and Circ., May 11, 1898.

[2] Norris and Landis: Diseases of the Chest, Phila., 1920, 2d edit.

*into the carotids; enfeeblement or obliteration of the second sound—at the base of the heart; and an infrequent pulse (pulsus rarus), with the wave of small amplitude (pulsus parvus) and much prolonged (pulsus tardus), and the artery well filled between the beats.*

The enlargement of the heart is not so pronounced as in aortic insufficiency. The apex beat, although sometimes weak, is usually forcible and deliberate. The thrill is present in the majority of cases. It is systolic, often intense, and, although generally best felt in the aortic area, it is widely distributed. As a rule, the murmur is loud and also widely propagated. In some instances it is louder to the left of the sternum in the second or third intercostal space than in the so-called aortic area. When aortic insufficiency coexists a diastolic murmur may also be heard over the base of the heart.

FIG. 30.—Sphygmogram showing a small, tardy pulse of the anacrotic type.

Owing to the narrowing of the aortic orifice and the forcible deliberate contractions of the left ventricle, the pulse is usually infrequent, with the wave small and prolonged. The sphygmogram may also show a pulse of the anacrotic or of the bisferiens type (see Fig. 30). In the anacrotic pulse the tidal wave is more pronounced than the percussion wave; in the pulsus bisferiens the summit of the wave is bifurcate, in consequence of the predicrotic fall being followed by a rise equal to or exceeding that of the percussion wave.

**Diagnosis.**—As a systolic murmur over the aortic area may be caused by a number of conditions, the diagnosis of aortic stenosis must never be made upon the mere presence of such a murmur. A positive diagnosis can be made only when a purring thrill, a feeble second sound and a characteristic pulse are also in evidence.

*Atheromatous roughening of the aorta or of the aortic cusps without obstruction* is a far more common cause of an aortic systolic murmur than actual narrowing of the aortic orifice. In these conditions, however, the second sound instead of being weak or inaudible is usually loud and ringing, a thrill is rarely present, and the pulse shows none of the characteristic features of aortic stenosis.

*Aneurysm of the aortic arch* may yield both a systolic murmur and a thrill, but in this lesion the second sound is accentuated, the pulse is unlike that of aortic stenosis, and furthermore, there are usually signs of a pulsatile tumor and symptoms of pressure upon adjacent structures. *Hemic* and *cardiopulmonary murmurs* can usually be excluded without difficulty (see p. 684). In *pulmonary stenosis* the murmur is not propagated into the carotid arteries, the cardiac dulness is increased to the right instead of to the left, the electrocardiogram reveals marked preponderance of the right ventricle, and the pulse is in no way characteristic.

## TRICUSPID INSUFFICIENCY

Tricuspid insufficiency is the commonest of the valvular lesions of the right side of the heart. In the large majority of cases it is caused by dilatation of the right ventricle and overstretching of the tricuspid ring. These changes in the right ventricle are most frequently secondary to mitral disease; in some cases they are the result of chronic pulmonary disease, such as emphy-

sema or cirrhosis of the lung; and in other cases they are due to uncomplicated myocardial weakness or degeneration. As the valve segments are normal the term relative tricuspid insufficiency is applied to this form of the disease. The escape of blood into the right auricle and venæ cavæ affords temporary relief to the overfilled right ventricle and pulmonary vessels, but it is another source of danger, since it opens the door to the evil consequences of general venous congestion.

Less frequently tricuspid insufficiency is caused by retraction and curling of the valve leaflets, the result of a previous attack of acute endocarditis, and in this case the aortic or mitral valve is usually similarly affected. Occasionally in ulcerative endocarditis the tricuspid is the only valve involved.

**Effects.**—As the right auricle during each systole of the ventricle receives more blood than under normal conditions it undergoes dilatation and hypertrophy. The right ventricle is usually already hypertrophied and dilated owing to coexisting mitral disease, but as during each diastole an abnormal volume of blood is discharged into it from the auricle, the hypertrophy and dilatation become more pronounced.

**Symptoms.**—The symptoms of tricuspid insufficiency are such as occur in other forms of valvular disease when the pulmonary and systemic veins become overdistended. Dyspnea, edema, cyanosis, and functional disturbances of the abdominal viscera are usually pronounced. Enlargement of the liver with pain and tenderness over the organ is often observed and not rarely there is slight jaundice.

The characteristic physical signs are *a pulsation in the jugular veins of the ventricular type, a systolic expansile pulsation of the liver, a systolic murmur of maximum intensity over the lower part of the sternum, and enlargement of the cardiac dulness to the right of the sternum.*

The venous pulse of ventricular form is of considerable significance, although it is not peculiar to tricuspid insufficiency and may be absent when this lesion is present. It may be seen in the internal and external jugular veins of both sides, although it is usually most pronounced in the right external vein. Rarely it is perceptible also in the superficial veins of the face and shoulder. If the venous pulse is due to an actual reflux of blood through an insufficient tricuspid valve the vein rapidly refills from below when it is emptied by stroking it from below upward and its upper extremity is then kept closed by pressure of the finger. (See p. 682.) In some cases the pulsation is propagated through the inferior vena cava into the hepatic veins, causing a rhythmic systolic increase and diastolic decrease in the size of the liver. This phenomenon is best appreciated by placing one hand in front over the lower border of the liver and the other behind over the eleventh and twelfth ribs. Impulses transmitted from an overacting heart or throbbing aorta are usually confined to the left lobe and are not expansile. The murmur of tricuspid insufficiency is not often propagated above the third rib nor more than an inch to left or right of the sternum. It is frequently obscured by a murmur due to mitral insufficiency. In the absence of an enlarged liver with systolic pulsation and rapid filling of the jugular vein from below after it has been emptied in the manner described, the recognition of tricuspid insufficiency as a complication or sequel of mitral insufficiency is possible only when there are two murmurs of different character and two areas over which these murmurs are especially loud.

## TRICUSPID STENOSIS

Tricuspid stenosis is rare. In 1888 Leudet[1] collected 114 cases with autopsies, in 1908 W. W. Herrick[2] collected 63 more, and in 1911 Futcher reported 5 of his own and cited 3 additional ones from the literature, making a total of 195 cases. Norris found 8 cases among 8640 autopsies at the Philadelphia General Hospital and Futcher 5 cases among 3500 autopsies at the John Hopkins Hospital. Of the 195 recorded cases 133 were in adults between 20 and 50 years of age, and at least 141 were in females. In only 14 cases was the tricuspid valve alone affected, mitral stenosis was the most frequent concomitant lesion. The diagnosis was made clinically in less than 7 per cent. of the cases. The disease may be congenital, but, as a rule, it develops after birth as a result of a previous attack of acute endocarditis due to rheumatism or chorea.

**Symptoms.**—Pronounced cyanosis is the most conspicuous feature, but dyspnea, edema, enlargement of the liver, etc. supervene sooner or later in the majority of cases. A diastolic or presystolic murmur with its point of maximum intensity over the lower part of the sternum and of a different quality from that heard at the apex is the most significant physical sign. This murmur is very often absent, however, owing to extreme weakness of the right auricle. Other important signs are a snapping first sound at the tricuspid area, an increase in the area of cardiac dulness toward the right, especially in the region of the right auricle, a presystolic or systolic thrill over the lower part of the sternum, a presystolic pulsation in the jugular veins and in the liver, polycythemia (8 or 9 million erythrocytes per cubic millimeter) and clubbing of the fingers. Upon the occurrence of decompensation and paralysis of the right auricle the presystolic pulsation in the jugular veins and liver almost always disappears. Shattuck believes that whether a diastolic or presystolic murmur can be heard or not tricuspid stenosis can be diagnosticated with a fair degree of certainty if the patient is a female with a rheumatic history, has mitral stenosis, perhaps also aortic disease, and presents the evidences of prolonged or recurrent venous stasis of greater or less degree. According to Levine,[3] in 3 cases of mitral stenosis proved at necropsy, all with mitral stenosis and auricular fibrillation associated, a striking feature clinically was the enlarged nonpulsating liver when there was no evidence either of cardiac failure or alcoholic cirrhosis.

## PULMONARY INSUFFICIENCY

Pulmonary insufficiency is a rare lesion. It may be congenital or acquired. The congenital form may be due to malformation of the valve segments or to intrauterine endocarditis. The acquired form may be secondary to some disease which has caused an abnormally high blood pressure in the pulmonary artery and widening of the pulmonary ring, such as mitral stenosis, or it may occur as a structural defect of the valve in the course of ulcerative endocarditis. Graham Steell[4] believes that relative insufficiency is not uncommon in cases of long-standing mitral stenosis. It is difficult, however, either to prove or to disprove this statement. The chief effect of pulmonary insufficiency is dilatation and hypertrophy of the right ventricle.

[1] Thèse de Paris, 1888.
[2] Arch. of Int. Medicine, 1908, ii, 291.
[3] Quoted by White, Jour. Amer. Med. Assoc., April 30, 1921.
[4] Diseases of the Heart, Manchester, 1906.

**Symptoms.**—The most trustworthy physical signs are a diastolic murmur, usually soft and blowing, heard loudest in the second or third left intercostal space near the edge of the sternum, and transmitted some distance downward, but inaudible in the vessels of the neck, and an increase in the area of cardiac dulness to the right of the sternum. Cyanosis is frequently present. Pulsations in the jugular veins, in the second left intercostal space (conus arteriosus) and in the epigastrium may also be observed. Dyspnea, often occurring in severe paroxysms, which are excited by exertion, is the most common symptom. Bronchitis, bronchopneumonia and other pulmonary complications are of frequent occurrence.

Pulmonary insufficiency may be distinguished from aortic insufficiency, the murmur of which is often heard loudest to the left of the sternum, by the absence of the Corrigan pulse and capillary pulse, by an increase in the cardiac dulness to the right rather than to the left, and by electrocardiographic evidence of right ventricular preponderance.

## PULMONARY STENOSIS

Pulmonary stenosis is almost always congenital and is usually associated with other cardiac defects, such as a patent foramen ovale or ductus arteriosus. Although rare, it is one of the most common of the congenital lesioins. An acquired form is very rarely observed as the result of acute endocarditis or of slowly developing sclerosis.

The physical signs consist of enlargement of the area of the cardiac dulness to the right of the sternum, electrocardiographic evidence of right ventricular hypertrophy, and a systolic murmur with its point of maximum intensity at the left edge of the sternum opposite the second rib or second interspace. The murmur is transmitted some distance upward, but it is not heard in the vessels of the neck. The second pulmonic sound is usually feeble or absent, although in the congenital form it may be normal or even accentuated if a patulous ductus arteriosus is also present. In many cases a systolic thrill may be felt in the second or third interspace to the left of the sternum. Cyanosis is usually a conspicuous feature in the congenital form, and accompanying it there may be polycythemia, clubbing of the fingers and toes, suffocative attacks, etc. In the acquired form there is little tendency to cyanosis and symptoms of venous stasis, such as dyspnea and edema, are, as a rule, late in appearing. Tuberculosis of the lungs is a common cause of death in subjects with congenital stenosis of the pulmonary orifice. The average duration of life does not exceed twelve years.

Before admitting the existence of so rare a lesion as pulmonary stenosis, a number of more common conditions producing a systolic murmur at the base of the heart should always be excluded. So-called *functional murmurs* are very frequently heard best in the pulmonic area and are usually systolic. These murmurs, however, are rarely accompanied by a thrill, and are not associated with cyanosis or enlargement of the right ventricle. The murmur of *mitral insufficiency* is sometimes loudest in the third left intercostal space, but unlike the murmur of pulmonary stenosis, it is usually propagated to the axilla and is associated with accentuation of the second pulmonic sound and enlargement of the left ventricle. The murmur of *aortic stenosis* is not rarely heard best to the left of sternum, but as distinguished from the murmur of pulmonary stenosis it is transmitted into the carotids and is accompanied by enlargement of the left ventricle and a characteristic pulse.

## COMBINED VALVULAR LESIONS

In a large proportion of all cases of valvular disease more than one lesion is present. As a rule, in such cases one of the lesions is predominant and the other is subordinate or secondary. Two or more valves may be diseased or there is insufficiency and stenosis at one valve. Aortic insufficiency is often associated with some degree of aortic stenosis and mitral stenosis is almost always associated with some degree of mitral insufficiency. The most common combinations, however, are those of aortic disease with relative mitral insufficiency and of mitral disease with relative tricuspid insufficiency. The diagnosis is often more difficult than in the case of single lesions and must be based upon a careful consideration of the areas in which the murmurs are best heard, the character and propagation of the murmurs, the secondary changes in the heart and other organs, and the quality of the pulse.

## PROGNOSIS OF CHRONIC VALVULAR DISEASE

In forecasting the course of a case of chronic valvular disease the important factors to be considered are the seat, nature, and extent of the lesion, the state of the cardiac muscle, the presence or absence of complications, and the age, sex, occupation and habits of the patients. All things being equal, the various left-sided lesions stand in the order of relative gravity as follows: first, aortic insufficiency; second, mitral stenosis; third, aortic stenosis; and fourth, mitral insufficiency. Too much stress, however, must not be put upon the seat and nature of the lesion as other factors may make these of secondary importance. Even aortic insufficiency, which is generally conceded to be the most serious of the more common valvular diseases, may last for many years, if the lesion is slight and quiescent and the nutrition of the heart muscle is good. Patients with well-marked mitral stenosis usually die before 40, but sometimes this lesion is met with at advanced ages. Tricuspid insufficiency, being as a rule a late sequel of some other disease, cardiac or pulmonary, is almost always a very serious lesion. Defects of the pulmonary valves are usually congenital and result in the death of the patient in infancy or by puberty. The character of the pathologic changes in the valve are no less important than the form of the defect. Thus, aortic insufficiency resulting from a previous attack of acute endocarditis is likely to be distinctly less dangerous than aortic insufficiency due to degenerative processes, as in the former the changes are usually stationary, while in the latter they are always progressive. In estimating the degree of obstruction or of insufficiency no reliance should be placed upon the loudness of the murmur. In the gravest cases, owing to weakness of the heart muscle, the murmur may entirely disappear; on the other hand, mere roughening of a valve may produce a murmur of great intensity. The condition of the myocardium is by far the most important factor in prognosis. If the degree of cardiac enlargement is slight and there are no evidences, subjective or objective, of myocardial weakness (see p. 647) the lesion admits, on the whole, of a hopeful prospect. If, however, there is marked enlargement of the heart and evidences of myocardial insufficiency are present, such as breathlessness following efforts which could previously have been made with ease, the prognosis must be guarded. Complications of all kinds make the outlook less favorable; such conditions as adherent pericardium, arteriosclerosis, chronic nephritis and pulmonary emphysema being especially effective in shortening the period of compensation.

Generally speaking, the prognosis of chronic valvular disease is most

favorable in youth and early manhood. In early childhood, owing to the frequency of concomitant pericarditis, and the liability to repeated attacks of rheumatism or chorea, each one of which may damage the heart still further, the outlook is less hopeful. Late in life, owing to the natural tendency to progressive degenerative changes in the heart and vessels, the outlook is also more or less precarious.

The influence of sex on the prognosis is difficult to determine. Women being less given to excesses and less exposed to the danger of heavy muscular effort are likely to retain compensation somewhat longer than men; but, of course, the stresses incident to pregnancy must be carefully considered, especially in mitral stenosis and aortic insufficiency. Occupation is a factor of considerable importance. Patients who can afford to live quietly under good hygienic conditions are obviously much better off than others who must engage in a laborious occupation, perhaps amidst unsanitary surroundings, that they may earn their daily bread.

After the actual appearance of symptoms of general venous congestion, the fatal termination is usually not far off, and yet under favorable conditions, it may be possible to restore the compensatory balance not only once, but many times. In this respect mitral disease is distinctly less serious than aortic. In any case, it is advisable to delay the prognosis until the effects of treatment have been determined. A remarkable degree of recovery may follow absolute rest and appropriate medication.

As to the question of cure, it is very doubtful whether the lesions of endocarditis are ever actually effaced; there is good reason to believe, however, that relative insufficiency of the auriculoventricular valves resulting from relaxation of the cardiac muscle may terminate in complete and permanent recovery.

### TREATMENT OF CHRONIC VALVULAR DISEASE

During the period of compensation the aim should be to promote in every way the nutrition of the heart muscle and to eliminate all conditions that may throw an undue strain upon the heart or that may increase the already existing valvular defect. The patient's whole manner of life must be carefully reviewed and his work, both mental and physical, his rest, his recreation, and his diet adjusted to the reserve power of his heart. Excesses of every kind should be avoided and emotional strain, anxiety and worry reduced to a minimum. The food should be nutritious and easily digestible. The importance of securing regular action of the bowels, of keeping the skin active by frequent bathing and of protecting the body by suitable clothing should be emphasized. Exercise in the fresh air should be encouraged, but whatever its nature, the amount should always be less than that which gives rise to sensations of discomfort. Finally, any focal infection, because of its power to depress the heart and to excite recurring attacks of endocarditis, should be removed, if possible.

After the occurrence of decompensation, the treatment resolves itself into that of myocardial insufficiency, which is fully considered on p. 651 et seq.

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## CONGENITAL ABNORMITIES OF THE HEART AND GREAT VESSELS

Congenital defects of the heart may be the result either of malformation or of intrauterine endocarditis. Endocarditic lesions are more common on the right side of the heart than on the left.

**Malpositions of the Heart.**—The most common and least serious of the malpositions of the heart is congenital dextrocardia, or transposition of the heart into the right side of the chest. In the majority of cases the lungs and abdominal viscera are also transposed (*situs viscerum inversus*). This anomaly can readily be distinguished from pseudo-dextrocardia, resulting from the pressure of left-sided effusions or the traction of right-sided adhesions. A much more serious form of malposition of the heart is *ectopia cordis*, a condition in which the organ is situated outside of the thorax, in the neck or in the abdominal cavity.

**Defects of the Cardiac Septa.**—Complete absence of the auricular septum is a rare deformity, and makes the heart a trilocular organ; or, in case the ventricular septum is also wanting, a bilocular organ. More commonly the septum is only in part deficient, and in this case the foramen ovale may be closed or patent.

A *patent foramen ovale* is a relatively common anomaly. It may exist alone; in which case no serious disturbance may follow. Generally, there are other abnormities, such as stenosis of the pulmonary artery or a defect in the ventricular septum.

Deficiencies in the ventricular septum may be complete or partial. In most cases the defect consists in small openings in the pars membranacea or "undefended space." Other abnormities are usually present, such as stenosis of the pulmonary artery or aorta, and a patulous ductus arteriosus or foramen ovale.

**Persistent Ductus Arteriosus.**—A pervious ductus arteriosus is a frequent accompaniment of septal defects and stenosis or atresia of the large vessels. When it exists alone, it is not incompatible with long life. Goodman in 1910[1] collected 71 cases and in 1915 Stoddard[2] collected 22 additional cases.

**Malposition of the Large Blood-vessels.**—Occasionally the pulmonary artery is derived from the left ventricle, and the aorta from the right ventricle. More frequently, from a deviation of the septum to the one side or the other, the two vessels have their origin in the same ventricle. These anomalies are usually associated with a patent foramen ovale and a pervious ductus arteriosus. Sometimes the septa are also defective.

**Malformation and Defects of the Valves.**—The most common valvular anomalies are those which affect the number and size of the segments. Union of the segments is occasionally encountered at the auriculoventricular valves, and may be the result of malformation or fetal endocarditis. There may be two or four semilunar cusps, instead of three; the presence of two is usually due to an ancient endocarditis that has altered two of the leaflets in such a way that they form one large pocket.

**Stenosis and Atresia of the Pulmonary Artery.**—Constriction of the pulmonary artery may be complete or partial; the former is rare, while the latter is one of the most frequent of the congenital heart lesions. The narrowing may involve the trunk of the vessel, the conus arteriosus, or the orifice. In many cases the ventricular septum is deflected considerably to the left, sometimes to such a degree that the aorta springs from the right ventricle. The latter cavity is usually enlarged. In the majority of cases the stenosis is associated with a patulous foramen ovale, an incomplete ventricular septum, and a pervious ductus arteriosus, through which the blood is carried into the lungs.

**Stenosis and Atresia of the Aorta.**—These are much less frequent than the corresponding lesions of the pulmonary artery. The orifice, the arch near

[1] Univ. of Penna. Med. Bull., Dec., 1910.
[2] Arch. Int. Med., July, 1915.

the ductus arteriosus, or the left conus may be the seat of constriction varying in degree from slight narrowing to complete obliteration. In marked stenosis or atresia of the orifice, the ventricular septum being impervious, the ductus arteriosus and the foramen ovale usually remain open, so that the right ventricle carries on both the systemic and pulmonary circulation through the pulmonary artery. In constriction of the arch between the ductus arteriosus and the left subclavian artery, the collateral circulation is effected by means of anastomosis between the branches of the subclavian and the descending aorta.

**Symptoms of Congenital Heart Disease.**—Cyanosis, of varying degrees, is the most constant and characteristic symptom. It occurs so frequently that the term "*blue disease*" was for a long time used to designate all malformations of the heart. The bluish discoloration usually appears within a few days or weeks after birth and persists through life. It is most marked, as a rule, in the lips, cheeks, nose, ears, hands and feet, and is intensified by crying, coughing, and other exertions. Accompanying the cyanosis there is a pronounced polycythemia. Clubbing of the fingers and toes is frequently present and also congestion of the abdominal organs. The temperature of the body is subnormal and patients often complain of a sensation of cold. Any act which increases the circulatory embarrassment is likely to cause dyspnea, cough and palpitation. Those who survive are usually poorly developed, sluggish in body and mind, languid and fretful. Examination of the blood almost invariably reveals an increase, in the number of red cells and percentage of hemoglobin. In Townsend's[1] 13 cases the red cells averaged 7,573,585 per cubic millimeter.

No satisfactory explanation of the occurrence of the cyanosis has yet been offered. Morgagni, Cruveilhier, Moreton Stillé, and others attributed it to venous congestion; Senac, Gintrac, and others to the intermingling of arterial and venous blood; and Peacock, to deficient aeration of the blood. The cause of the polycythemia is also a matter of dispute.

**Physical Signs.**—The most characteristic physical signs are a loud systolic murmur, audible over the entire precordium but most intense at the base; a palpable thrill, also most marked at the base; and increase of the area of cardiac dulness, especially to the right.

In uncomplicated pulmonary stenosis, in addition to these signs, there is usually enfeeblement of the pulmonic second sound. If the second sound is much accentuated it is probable that patulous ductus arteriosus is also present. In both deficiency of the intraventricular septum and patent ductus arteriosus the murmur is often extremely loud and prolonged, beginning early in systole and continuing into diastole (brûit de Roger). Persistence of the foramen ovale as an isolated lesion may exist without symptoms or physical signs.

**Prognosis and Termination.**—The prognosis is variable, but, on the whole, unfavorable. Many patients die within a few days or weeks and at least 50 per cent. succumb during the first five years of life. Of those who live to adolescence, a large proportion develop pulmonary disease, especially tuberculosis. Secondary endocarditis is also common. In individual cases, the outlook is unfavorable in proportion to the degree of cyanosis, dyspnea and general malnutrition. Defects in the auricular or ventricular septum and patulous ductus arteriosus, if uncomplicated and without severe symptoms, often permit of life into adult years.

[1]Archives of Pediatrics, Sept., 1899.

## PERICARDITIS

**Etiology.**—Excepting in the very rare instances in which it follows direct trauma, pericarditis is always a secondary process. Clinically four groups of cases may be recognized.

(1) Cases secondary to a general infection, such as acute rheumatism, chorea, pneumonia, pyemia, scarlet fever, cerebrospinal meningitis, etc. (2) Cases developing in the course of a chronic disease, such as chronic nephritis, leukemia, scurvy or diabetes, which has lowered the resistance of the tissues and made invasion by microörganisms of easy occurrence. (3) Cases secondary to disease of an adjacent structure, such as pneumonia or pleurisy of the left side, myocarditis, infected mediastinal or peribronchial lymph-nodes, ulceration of the esophagus, caries of the ribs or sternum, aneurysm of the thoracic aorta, occlusion of the coronary arteries by an embolus or thrombus, gastric ulcer, etc. (4) Cases in which there is a definite infection atrium more or less distant from the heart, as in the tonsils, an abscess, an infected wound or burn. The organisms most frequently found in the exudate are the pneumococcus, streptococcus, staphylococcus, and tubercle bacillus. The invasion of the pericardium may occur in one of the following ways: (*a*) through the blood-stream, (*b*) through the lymph vessels, (*c*) by extension from adjacent structures, and (*d*) by direct injury.

*Rheumatism* is the most common cause of the disease. Of 100 cases analyzed by Sears[1] 51 were associated with rheumatism. Estimates of the frequency with which the pericardium is involved in rheumatism vary 6.6 per cent. (Osler) to 24 per cent. (Pye-Smith). Zinn[2] observed pericarditis in 10 per cent. of 1000 cases of rheumatism. In children the proportion is larger than in adults. While pericarditis may develop in the mildest type of rheumatism, there seems to be greater liability to it when several joints are affected and the constitutional symptoms are severe. Rarely it precedes the arthritis or is the only manifestation of the rheumatic infection.

*Pneumonia* was the cause in 18 of Sears 50 cases and in at least 29 of 71 cases analyzed by Wells. According to Chatard,[3] of 665 cases of lobar pneumonia 31, or 4.6 per cent. were complicated with pericarditis. Pneumonia is undoubtedly the most common cause of pericarditis in children under 4 years of age and of purulent pericarditis at any age. The pericarditis is usually associated with metapneumonic pleurisy, but it may develop independently. Pericarditis from pneumococci has occasionally been observed without pneumonia. The incidence of the disease is much higher in streptococcus pneumonia than in pneumococcus pneumonia.

*Nephritis* is one of the most important causes of the disease in adults, especially in persons past middle life. While the complication is most frequent with chronic glomerulonephritis and the cirrhotic kidney, it also occurs with tubular nephritis, both acute and chronic. It is probably always to be ascribed to a secondary or terminal infection, although some observers, like Banti, failing to demonstrate organisms in the effusion, still believe with Lancereaux that it may result from uremic intoxication. The effusion of nephritic pericarditis is usually serofibrinous, but it may be purulent.

*Tuberculosis* is a comparatively rare cause of pericarditis. Norris[4] found 82 cases among 7219 general necropsies, 1780 of the latter being on clinically tuberculous subjects. Among 337 necropsies at the Phipps Institute for the Study of Tuberculosis[5] pericardial tuberculosis was found but

[1] Boston Med. and Surg. Jour., April 22, 1897.
[2] Therap. der Gegenwart, 1909, I, No. 9.
[3] Johns Hopkins Bull., Oct., 1905.
[4] Univ. of Penna. Med. Bull., July-Aug., 1904.
[5] Fifth Annual Report, 1907, 336.

3 times. The process may be of an acute type, although it is usually chronic and serofibrinous or obliterative.

**Morbid Anatomy.**—Inflammation of the pericardium is invariably accompanied by more or less exudation, and according to the character of the latter three varieties of the disease may be distinguished: serofibrinous, hemorrhagic, and purulent.

*Serofibrinous Pericarditis.*—In this form the membranes first become injected and lusterless; and then covered with a variable amount of fibrin. The latter may be limited in distribution to the auriculoventricular grooves or the posterior wall of the ventricles, but in many instances it is wide spread and involves the whole surface of the heart. When newly formed it is soft and can readily be detached; when old it is firm and tenacious. On account of the constant movement of the heart, it often prevents a shaggy, tripe-like or velvety appearance.

The deposition of fibrin is accompained by a serous exudation, the quantity of which sometimes reaches one or even two liters. Such large effusions would certainly be incompatible with life were it not that the inflammatory process greatly increases the distensibility of the pericardium. The fluid may be quite clear, but, as a rule, it is more or less turbid from the presence of leucocytes and fibrin.

The term *dry pericarditis* is applied to the cases in which the serous exudation is inconsiderable and the fibrinous deposit amounts to no more than a delicate pellicle.

Although serofibrinous pericarditis may end in a complete restoration of the serous surfaces to a normal condition, this is not likely to occur if there is considerable fibrin. In such cases the fibrin is usually replaced by fibrous tissue, the sac becoming partially or wholly obliterated (*chronic adhesive* or *fibrous pericarditis*). Circumscribed deposits instead of resulting in adhesions sometimes leave behind on the surface of the heart the white opaque patches known as "milk-spots."

The most common causes of serofibrinous pericarditis are rheumatism, chorea, chronic nephritis and tuberculosis.

*Hemorrhagic Pericarditis.*—The only difference between this form and the preceding is that the effusion contains a variable proportion of blood. Hemorrhagic effusions are relatively more frequent in the pericardium than in the pleura. They are encountered most often in tuberculosis, but they are not rare in chronic nephritis, scurvy, and chronic alcoholism.

*Purulent Pericarditis.*—Pneumonia is the most important cause of this form of pericarditis, but general pyemic infection, suppurating processes in adjacent structures, and the acute specific fevers not infrequently excite it. It is more common in children than in adults. The amount of pus varies from a few hundred cubic centimeters to a liter or more. A variable quantity of soft fibrin is usually found floating free in the pus or attached to the surface of the heart. A large proportion of the cases terminate fatally. Spontaneous discharge of the pus through the chest-wall or into the esophagus, pleura or bronchi occasionally occurs. Recovery without operation, the pus becoming inspissated and ultimately calcified, is a rare termination. Artificial evacuation of the pus, when successful, results in fibrous union, partial or complete, of the pericardial surfaces.

**Associated Conditions.**—In all forms of pericarditis the myocardium is more or less involved. If the muscular lesions are extensive they may be much more potent in producing grave sequels than the disease of the pericardium itself. Endocarditis is frequently present, especially in children, and results from the same cause as the pericarditis. Dilatation of the heart occurs in severe cases as a result of the myocardial changes.

**Symptoms.**—While the development of pericarditis is frequently marked by a sudden rise of temperature (102°–103° F.), and more or less pain in the cardiac region, these symptoms are not rarely wanting, especially in subacute cases. The pain, which is usually limited to the precordium, may be sharp and stabbing or merely a sense of oppression. Occasionally, if the heart itself is much affected, it is of an anginoid character. In some cases the pain is accompanied by tenderness on pressure.

The pulse is accelerated, sometimes reaching 140 or 150 a minute. In severe cases it soon becomes small and weak. Occasionally it is paradoxic. Marked irregularity of the pulse is usually indicative of associated myocardial lesions. Dyspnea is a variable symptom. When the effusion is copious or is produced quickly or the heart itself is much affected, it may be very severe, necessitating a sitting posture.

The face is frequently pale and anxious or distinctly cyanosed. Attacks of faintness are not uncommon. Hoarseness or aphonia from compression of the recurrent laryngeal nerve, irritative cough from compression of the trachea, and dysphagia from compression of the esophagus are occasional symptoms. In grave cases nervous phenomena—extreme restlessness, delirium, and stupor may be a prominent feature. Almost all cases, except the tuberculous, show polymorphonuclear leucocytosis (10,000–30,000).

**Physical Signs.**—The first and most characteristic sign of pericarditis is a friction-sound, produced by the rubbing together of the roughened serous surfaces. In most cases this sound is heard loudest where the body of the heart is most superficial, that is in the third or fourth left intercostal space, although it may be heard with maximum intensity over any part of the precordium. In not a few cases the site of the rub changes from day to day—a point of considerable diagnostic import. Generally, it is a to-and-fro sound occurring with each act of the heart, but it is rarely synchronous with the normal cardiac sounds, indeed, the latter are often heard in addition to the friction. Occasionally, it occurs only with one act of the heart, or it may be at one time systolic and at another diastolic. It is a rough, grating, or scraping sound, likened to the creaking of new leather or the noise produced by rubbing together two pieces of stiff paper. It gives the impression of having a very superficial origin, and moderate pressure of the stethoscope may prolong or intensify it. It is often modified by position and also, to a slight extent, by respiration. The area over which it is audible is usually very limited, and in exceptional cases only is it propagated beyond the area of the heart dulness. In many cases it gradually disappears as the fluid in the sac accumulates, but sometimes it persists even after a large effusion has formed. Finally, there are cases, especially of the purulent variety, in which the friction sound is absent or eludes detection throughout the entire course of the disease. In a small proportion of cases a friction-fremitus is felt at the point where the friction sound is best heard.

Increased prominence of the precordial region with widening and bulging of the intercostal spaces is a sign of considerable importance, but it is often absent, especially in adults, even when the effusion is large. With the accumulation of the fluid the apex beat, as a rule, gradually decreases in force until it is no longer visible or palpable. However, if the effusion is not excessive a pulsation may sometimes be detected in the fourth or even the third interspace, although this is not the apex impulse. Occasionally, the heart is pushed forward by an accumulation of fluid behind it, and as a result the apex impulse remains unchanged.

Pulsation of the vessels of the neck is occasionally as pronounced as it is in aortic disease (Stokes, Huchard).

Palpation serves to confirm the results of inspection. Further, in extensive effusions, owing to the great activity of the upper respiratory region of the chest, the left clavicle may be raised to such an extent, that it is possible to feel the upper edge of the first rib as far as its sternal attachment (Ewart's first rib sign). Too much reliance, however, should not be placed upon this sign as it may occur also in cardiac enlargement.

Percussion gives the most trustworthy evidence of effusion. With the distention of the sac there is an increase in the area of precordial dulness. The shape of the dull area is not always characteristic, but when the effusion is considerable it is usually that of a pear with the butt-end downward. Important points in differential diagnosis are the early appearance of absolute dulness over the sternum and the extension of the dulness (a) upward as high as the second intercostal space or higher, (b) to the left beyond the position of the apex-beat, and especially (c) into the fifth right intercostal space or the cardiohepatic angle (Rotch's sign). The right border of cardiac dulness on approaching the liver dulness, instead of projecting vertically downward or curving inward, as is the case with the normal or a dilated heart, spreads obliquely outward, thus making the cardio-hepatic angle obtuse, rather than acute or right angled (Ebstein's sign). The upper portion of the left lung being relaxed yields a note that is more or less tympanitic and for this reason the left border of the area of cardiac dulness is often sharply defined. Compression of the left lung sometimes gives rise to an area of dulness posteriorly in the region about the angle of the left scapula. This area may be smaller when the patient leans well forward than when he sits upright. With large effusions there is often a marked downward displacement of the liver.

On auscultation, the heart sounds are observed, as a rule, to become progressively more indistinct and muffled as the fluid accumulates. Occasionally, however, the heart sounds, as well as the friction, persist even when the quantity of effusion is large. Over the dull area about the angle of the left scapula bronchial breathing and bronchophony may often be heard.

The roentgen ray is a valuable aid in detecting pericardial effusion, but, of course, its employment is not always feasible.

**Purulent Pericarditis.**—The symptoms and physical signs are the same, in the main, as those of serofibrinous pericarditis. The friction sound, however, is not rarely absent or present for so short a time that it is readily overlooked. Persistent, irregularly remittent fever, sweating, and rigors, when present, indicate the presence of pus, but in many cases these aids to diagnosis are wanting. Intense pallor is suggestive. Edema of the chest-wall is even more rare in pyopericardium than in empyema. Frequently exploratory puncture affords the only means of determining the exact character of the fluid.

**Diagnosis.**—An *endocardial murmur* may sometimes be mistaken for a pericardial friction, but the former is heard loudest at one of the valve areas; it coincides accurately with a particular phase of the cardiac cycle; it seems less superficial than the friction; it is frequently propagated beyond the area of the precordium; it is not modified by pressure of the stethoscope; and it is less likely to vary in rhythm, location and character from day to day.

As a rule, no difficulty is experienced in distinguishing between a pericardial and a *pleural friction sound*, as the latter is synchronous with

the respirations and ceases when the breath is held. Some confusion may arise, however, if the pleura adjacent to the pericardium is involved, but even in this case it will usually be observed that the friction is heard only at the border of the cardiac dulness and is considerably modified by a full inspiration or a full expiration.

The differential diagnosis between pericardial effusion and *dilatation of the heart* is sometimes very difficult, especially if the patient is first seen at a late period. Attention to the following points will, however, usually lead to a correct opinion. In dilatation the cardiac impulse is commonly visible and widespread; the apex-beat is sometimes displaced downward; the area of dulness is increased laterally rather than upward, and in form is not often definitely pear-shaped; the percussion note over the left lung is not vesiculotympanitic and consequently the left border of the cardiac dulness is not so sharply defined as in pericardial effusion; the angle formed by the heart and liver, instead of being obtuse is usualiy a right angle; and the heart sounds, though short, are distinct rather than muffled and distant.

**Prognosis, Course and Terminations.**—The prognosis depends upon the nature and severity of the attack. Cases of serofibrinous pericarditis occurring in the course of rheumatism or chorea, and in which the effusion is not very large and is not attended with severe cardiac or respiratory embarrassment, usually progress to a rapid and complete recovery. Nevertheless, in view of the difficulty in determining the extent of the fibrinous deposit and the degree of involvement of the myocardium, the prognosis should be guarded. Not rarely, adhesions partial or complete, occur between the two layers of the pericardium, and symptoms of cardiac dilatation eventually supervene.

Pericarditis that is secondary to chronic nephritis usually runs a short course, and is almost invariably fatal. This is true, also of the acute tuberculous form. In all cases of purulent pericarditis the outlook is grave, although, if the septic process is confined to the pericardium, early surgical intervention affords a definite chance of recovery. The duration of acute pericarditis is variable. Ordinary cases of rheumatic origin usually terminate by absorption in two or three weeks. On the other hand, in severe attacks death may occur within a few days as a result of mechanical interference with circulation due to a sudden increase in the intrapericardial pressure. In some instances the disease lasts for months, the issue being slow convalescence, or death in consequence of exhaustion or of cardiac dilatation, with all the symptoms of general venous congestion.

**Treatment.**—Absolute rest of body and mind is essential. During the first week, at least, milk is the most suitable form of nourishment. Of local applications, none is so generally useful in allaying pain and palpitation as the ice-bag. If cold is not well borne hot fomentations may be substituted. In cases with very severe pain the application of a few wet cups or of a fly-blister frequently affords relief. Morphin is sometimes necessary. In addition to relieving pain, it lessens restlessness and promotes sleep. In rheumatic cases salicylates should be continued. The routine administration of cardiac stimulants is objectionable, but such drugs as digitalis, caffein, and camphor, are necessary when signs of cardiac weakness develop.

*Stage of Effusion.*—In the serofibrinous cases if the exudate is slight and causes no discomfort, an expectant plan of treatment may be safely employed. If the effusion is considerable, but is without serious effects upon the heart treatment by counterirritation, a dry diet, and the administration of purgatives and diuretics may be tried, although it frequently fails of its purpose.

If the effusion proves menacing or persists after a thorough trial of medic-

inal treatment, paracentesis pericardii should be performed. As to the best site of the puncture, there is no uniformity of opinion. The point most commonly recommended is the fifth left intercostal space, to the outside of the internal mammary artery, or about one inch from the border of the sternum. A point equally good, if not better, especially if the heart sounds and friction are well heard, is in the fifth intercostal space just inside the lateral border of cardiac dulness. A puncture at this point is not likely to enter the pleura, as the lung is usually pushed well to the left by the effusion. Another point recommend by some writers is the left costo-xiphoid angle, the needle being thrust upward and backward close to the costal margin. A preliminary incision through the skin under local anesthesia is advisable if pyopericardium is suspected. Puncture of the right ventricle has not been infrequent in attempts at paracentesis. Fortunately, however, this accident has rarely caused serious consequences, although Broadbent[1] cites two instances in which it resulted fatally through hemorrhage. It is unnecessary, and often inadvisable, to withdraw all of the effusion. The removal of a portion lessens the pressure within the sac and thus permits the remainder to be absorbed.

In pyopericardium free incision with drainage is indicated, and paracentesis should be restricted to diagnostic purposes. The mortality of cases treated surgically is at least 50 per cent.

The period of convalescence requires careful attention. The absolute rest should be continued until all evidences of the disease have disappeared, and for many months afterwards no effort should be permitted that is likely to cause the least cardiac strain.

## CHRONIC ADHESIVE PERICARDITIS

Chronic adhesive pericarditis is usually a sequel of acute pericarditis, but it may develop insidiously in consequence of a subdued infection, which probably in some cases is tuberculous. According to the extent and distribution of the adhesions the cases may be grouped in the following classes: (1) Those in which only a few long or short fibrous bands (synechiæ) exist between the visceral and parietal layers of the pericardium; (2) those in which the pericardial surfaces are universally adherent, the sac being completely obliterated; (3) those in which there are not only intrapericardial adhesions, but also external adhesions uniting the sac to the pleura, mediastinal tissues, chest-wall or diaphragm (*chronic mediastino-pericarditis*); (4) rare cases in which there are extra-pericardial adhesions, but the two layers of the pericardium are free.

Adhesive pericarditis, especially mediastino-pericarditis, is often associated with considerable hypertrophy of the heart, the cause of which has evoked much discussion. In the majority of cases the enlargement is probably due to the myocardial changes or valvular defects, which so often accompany exudative pericarditis. It seems likely, however, that in some instances interference with the contractions of the heart or strangulation of the great vessels also plays a part. In the absence of endocarditis or arteriosclerosis the heart-weight is frequently within normal limits.

In some instances chronic adhesive pericarditis is a part of a general serositis (Pick's disease), in which the pericardium, pleura, and peritoneum become involved in varying combinations.

In regard to the incidence of adherent pericardium, W. H. Smith[2] found 62 cases of the disease in 3053 necropsies.

[1] Broadbent, Heart Disease, 1900.

[2] Jour. Amer. Med. Assoc., Sept. 6, 1913.

**Symptoms.**—Chronic adhesive pericarditis often fails of recognition. Partial adhesions may cause little or no interference with the function of the heart, and even complete obliteration of the pericardium, if unaccompanied by valvular or vascular lesions, may be "latent." Of the 62 cases of chronic pericarditis, with partial or complete adhesions, analyzed by W. H. Smith[1] 26 were symptomless. When symptoms occur they are chiefly the result of myocardial changes and may not differ in any way from those that the coexisting valvular disease might produce. Thus, there may be palpitation, dyspnea, cough, cyanosis and edema. Pain in the region of the heart is not uncommon and occasionally it is of an anginoid character. In some cases the symptoms simulate those of cirrhosis of the liver (pericarditic pseudocirrhosis of the liver) and consist of gradual enlargement of the liver, general weakness, ascites, edema of the legs and, perhaps, hydrothorax.

**Physical Signs.**—Bulging of the precordium is frequently seen, especially in children. The area of pulsation is usually much increased. Systolic retraction about the apex, over a large part of the precordium, or at the base of the left chest posteriorly, in the region of the eleventh and twelfth ribs (Broadbent's sign), is sometimes observed, and is suggestive of adhesions, although it may occur also with marked hypertrophy of the heart. At the close of the systolic tugging a distinct rebound (diastolic shock) is occasionally noted. Deficiency in the respiratory movements to the left of the sternum and over the upper part of the abdomen on the left side may sometimes be detected both by the eye and the hand and not rarely the position of the apex-beat becomes fixed, not shifting vertically with deep respiration or laterally with change of posture, but both of these signs may be present also in simple chronic pleurisy with adhesions. As pointed out by Kussmaul,[2] the radial pulse sometimes becomes very weak or even imperceptible during deep inspiration (*pulsus paradoxus*). When present in adherent pericardium, this phenomenon is probably due to tightening of adhesions about the larger vessels during full expansion of the chest. As it may occur in pericardial effusion without adhesions, in extreme weakness of the heart, in stenosis of the air-passages and in rare instances even in health, it is not a reliable indication. The same may be said also of the sudden diastolic collapse of the veins of the neck described by Friedreich. Reduplication of the second sound at the base is common, but it is relatively unimportant. Cardiac murmurs, the result of coexisting valvular disease, are frequently present, particularly at the mitral or tricuspid area. In an analysis of 46 cases in which a presystolic murmur occurred at the apex in the absence of mitral stenosis, Phear[3] found that adherent pericardium was present in 20. Finally, in some cases of adhesive pericarditis the x-ray gives important diagnostic evidence.

**Diagnosis.**—This is often a matter of considerable difficulty. The condition may be suspected, however, when several of the signs that have been mentioned are present, and especially when rheumatism followed by endocarditis appears in the history and the cardiac failure is more marked or the cardiac enlargement more extensive than the endocardial damage seems to warrant (W. H. Smith).

**Prognosis.**—The prognosis is virtually that of the associated myocardial condition, and depends largely upon the degree of efficiency shown by the heart under effort. After the occurrence of decompensation the outlook is, as a rule, grave, as the response to treatment is poor in comparison

[1] Jour. Amer. Med. Assoc., Sept. 6, 1913.
[2] Berlin. klin. Woch., 1873, No. 37.
[3] Lancet, Sept. 21, 1895.

with that observed in most cases of valvular disease with evidences of cardiac failure.

**Treatment.**—When symptoms of heart failure supervene the treatment is that of decompensation in valvular disease. In 1902 Brauer[1] suggested that in cases with well marked physical signs and without complications it would benefit the patient to remove some of the bony and cartilaginous framework of the thorax over the heart. He termed the operation, which does not require penetration of the pericardium, *cardiolysis*. The procedure, although a somewhat formidable one under the circumstances, has proved effective in a number of instances. Of 38 cases collected by Delagenière[2] good results were obtained in 31. It is probable, of course, that many unfavorable results have not been recorded. The operation is contraindicated in tuberculous cases and in those in which the disease is a part of a general serositis.

### ADHERENT PERICARDIUM WITH ASCITES

**(Multiple Serositis; Polyorrhomenitis)**

In 1896 Pick[3] described under the caption "pericarditic pseudocirrhosis of the liver" three cases in which obliterative pericarditis was associated with enlargement of the liver and ascites of long duration. At necropsy perihepatitis (the "sugar-iced liver" of Curschmann) was a constant finding. The liver itself in two cases showed some degree of cirrhosis, and in the other an extreme grade of chronic venous congestion (nutmeg liver). Other cases were afterward described by various writers, and in 1903 Kelly[4] collected 39 cases from the literature. The chief features are ascites with little or no edema of the legs, enlargement of the liver (in advanced cases the liver may be small) and recurrent attacks of perihepatitis. The ascites, as a rule, is marked and requires frequent tapping. The cardiac features are often inconspicuous; enlargement of the spleen is absent or of late occurrence; and jaundice is rare. In many cases a chronic adhesive pleurisy or a serofibrinous pleurisy which requires repeated aspiration is also present.

Pick assumed that the obliterative pericarditis was the primary condition and that the ascites was due to a cirrhosis of the liver resulting from long-standing venous congestion. This view is probably correct in some instances. In the majority of cases, however, the pericarditis, peritonitis (perihepatitis), and pleuritis are undoubtedly independent expressions of a primary infectious process of slight virulence which affects simultaneously or consecutively several serous membranes (general serositis). Not rarely, both a perihepatitis and changes in the liver secondary to obliterative pericarditis seem to be concerned in producing the ascites, which is usually the most obtrusive feature of the disease.

The etiology of the condition is obscure. Some of the cases are undoubtedly tuberculous. A history of acute rheumatism is occasionally obtainable.

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## HYDROPERICARDIUM

Hydropericardium, or dropsy of the pericardium, is an excessive accumulation of non-inflammatory fluid in the pericardial sac. It is usually

[1] Münch. med. Woch., 1902, xlix, 982.
[2] Arch. d. mal. du cœur, 1913, vi, 633.
[3] Zeitschrift. f. klin. Med., 1896, Bd. xxix, S. 385.
[4] Amer. Jour. Med. Sci., Jan., 1903.

observed in association with hydrothorax, ascites and anasarca, in the course of chronic cardiac disease with decompensation or chronic nephritis, but occasionally it is found as an independent effusion arising from pressure upon the veins of the pericardium or heart by a tumor, aneurysm, enlarged lymph-nodes, or adhesions. The symptoms are usually masked by those of the primary condition. The physical signs are those of pericarditis with effusion. It may be distinguished from the latter by the history of the case, the symptoms of the underlying causal condition and the absence of friction sounds.

## HEMOPERICARDIUM

An accumulation of blood in the pericardial sac may result from a penetrating wound of the pericardium or heart, from spontaneous rupture of the heart, from the rupture of an aneurysm of the aorta, the pulmonary artery or a coronary artery, or from erosion of the pericardium by a malignant growth. In pericarditis from tuberculosis or occurring in the course of cachectic states the effusion is frequently mixed with a variable amount of blood.

The combined symptoms of internal hemorrhage and of a liquid accumulation in the pericardium, together with the history of the case may lead to a correct diagnosis. Death may occur at once or within an hour or two, but in some cases life is prolonged for several days. In a number of cases traumatic hemopericardium has been successfully treated by laying open the sac, evacuating the blood and suturing the heart muscle.

## PNEUMOPERICARDIUM

The accumulation of gas in the pericardium is a rare condition. Of the 38 cases collected by James[1] 19 were the result of traumatism, the pericardium having been torn by a penetrating wound of the chest, a fractured rib, or a foreign body impacted in the esophagus. The next most frequent cause has been perforation of the pericardium by an ulcerative process in an adjacent air-containing organ; thus, it has followed pyopneumothorax, tuberculosis or gangrene of the lung, ulcer or cancer of the esophagus and ulcer of the stomach. A few cases appear to have resulted from an infection of the sac by a gas-producing bacillus (*Bacillus aërogenes capsulatus*), without perforation. The presence of air is almost invariably productive of a serous or purulent effusion.

The *symptoms* of pneumopericardium are much the same as those of pericarditis with copious effusion, the physical signs alone being distinctive. The most characteristic sign is a splashing, churning, or gurgling sound ("mill-wheel" sound), synchronous with the heart-beats, and occasionally audible several feet away from the patient. This sound is sometimes accompanied by a metallic tinkling, which is also synchronous with the movements of the heart. Percussion over the precordium reveals an area of tympanitic resonance, which varies in site and extent according to the position of the patient. With the patient prone the whole area of cardiac dulness is replaced by a tympanitic note, and with the patient sitting up,

[1] American Medicine, July 2, 1904.

the upper portion of the precordium is tympanitic and the lower portion dull. Not rarely, too, the apex beat, disappears when the patient assumes the recumbent position and reappears when he sits up. In several instances radiographic or fluoroscopic examination has proved useful in diagnosis. In Ljungdahl's[1] and in Cowan's[2] case the condition was recognized only on examination with the x-ray.

The **prognosis** of pneumopericardium is very grave, although 11 of James's cases (8 of the 19 traumatic cases) ended in recovery.

# DISEASES OF THE ARTERIES

## ARTERIOSCLEROSIS

(Atheroma; Atherosclerosis)

Arteriosclerosis is a chronic disease of the arterial system in which the vessels tend to become thicker, harder, and less elastic than normal as a result of structural changes, which are in part degenerative and in part productive.

When the disease affects chiefly the aorta and larger arteries and the degenerative changes are dominant it is often spoken of as *atheroma*. The term *arteriocapillary fibrosis*, introduced by Gull and Sutton, is sometimes employed to designate the process when it involves the capillaries as well as the arteries. Von Basch suggested the name *angiosclerosis* for the condition when it affects the entire vascular system, including the veins.

**Etiology.**—Arteriosclerosis is a natural concomitant of *senescence*. This involutionary form of the disease is rarely pronounced, before the sixth decade of life, although the time of its occurrence is largely determined by heredity and mode of living. Some persons inherit arterial tissue of low resistance and then even the ordinary wear and tear of living may exhaust the vitality of the vessels long before the conventional three-score years and ten. Again, those who live under conditions in which stress is particularly severe often develop senile changes in their vessels at a comparatively early period.

The causes which favor premature arteriosclerosis operate chiefly through the blood, either by increasing its distensive force or by effecting changes in its composition. That *mechanical strain* itself may be an etiologic factor is confirmed by the fact that vessels and parts of vessels which are most subjected to insults of the blood stream are the earliest and most severely affected, and also by the fact that the disease develops so frequently and so soon in persons who are engaged in laborious occupations. While *hypertrophy of the heart* is frequently a result of general arteriosclerosclerosis, it may also favor the occurrence of the disease, especially in the larger vessels, increased blood pressure again being the determining factor.

*Certain chronic intoxications*, such as occur in chronic nephritis, gout, and diabetes, are common causes of arteriosclerosis. In these cases it is conceivable that the morbific agent may act by injuring the arterial tissues directly or by contracting the peripheral vessels, and thus increasing the blood pressure.

Alcoholism, lead-poisoning and tobacco-poisoning are also commonly held responsible for the disease, but this seems to be only an impression and

[1] Deutsch. Arch. f. klin. Med., 1913, cxi, 19.
[2] Cowan: Diseases of the Heart, Phila., 1914, p. 420.

lacks the support of scientific evidence. The suggestion that hypertension due to excessive activity of the suprarenal glands may produce arteriosclerosis has not been proved. Repeated anaphylactic shocks from the absorption of proteins to which the individual has become sensitized are a possible, but unproved, cause of the condition.

*Syphilis* plays a very important rôle in the etiology of one form of the disease, which has been termed a mesarteritis. The Spirochæta pallida has been found in the lesions. Whether the luetic poison itself is capable of producing other forms of arteriosclerosis is not known. It is probable that the *acute infectious diseases* sometimes produce, as in the case of chronic myocarditis, changes in the arteries which become the foundation of a subsequent sclerosis. *Sedentary habits* by deranging metabolism and interfering with elimination seem to favor early arterial degeneration. Finally, there are cases in which *intemperance in eating* is the only factor (Osler).

**Morbid Anatomy.**—Four varieties of arteriosclerosis may be recognized: The nodular, the senile, the diffuse, and the syphilitic.

*Nodular Form.*—This affects chiefly the aorta and larger arteries.

In the early stages of the process the inner surface of the vessel presents irregular, slightly elevated plaques, translucent and somewhat gelatinous in appearance. Later, these plaques are firm and almost cartilaginous. When old they are yellowish-white and opaque from calcification and degeneration. In some cases a plaque is transformed by extensive calcification into a projecting brittle plate; in other cases, as a result of necrosis, it is converted into a pulpy mass of fatty detritus, which ultimately escapes into the blood stream, leaving behind a so-called atheromatous[1] ulcer.

Microscopically, the changes in the intima consist primarily of a marked proliferation of the subendothelial connective tissue. The fusiform and stellate cells constituting the hyperplasia are at first well-defined, but gradually they undergo degeneration and are replaced by oil drops, cholesterin crystals, and granular detritus. Calcification also occurs. The media under the plaques is usually more or less thinned and fatty.

*The Senile Form.*—This may affect any part of the arterial tree, but as a rule it produces its most characteristic changes in the radials and other middle-sized arteries, which in advanced cases are transformed into narrow, rigid tubes resembling pipe-stems.

The aorta is often the seat of sclerotic plaques (nodose arteriosclerosis), but in uncomplicated cases its wall is thinned rather than thickened and the vessel is more or less distended and tortuous. A striking feature in many cases, as Mönckeberg[2] has shown, is the presence of slight sacculations in the main branches of the aorta, due to giving way of the media. Microscopically, the media shows fatty degeneration and atrophy of the muscle cells and elastic fibers, and at a later period fibrosis and calcification, and the intima, at first, hyperplasia of the connective tissue and elastic fibers, and later, if the condition is sufficiently advanced, fatty degeneration of both of these elements.

*The Diffuse Form.*—This form, which corresponds to the arteriocapillary fibrosis of Gull and Sutton, is observed most frequently in association with chronic nephritis and essential hypertension. It affects especially the smaller vessels, causing thickening of their walls and contraction of their lumina. Microscopically, the changes resemble those of the senile form, but the hyperplastic part of the process is much more pronounced than the fatty or calcific.

[1] Atheroma is from the Greek, ἀθήρη, pap or porridge.
[2] Virchow's Archiv., 1903, clxxi, 141.

*The Syphilitic Form.*—This form may affect any of the arteries, although it has a strong predilection for the ascending aorta and arch. When the affected vessel is laid open its lining is found to be thrown up into sharply defined, translucent or opaque nodular swellings or into numerous longitudinal folds. These elvations, as contrasted with the plaques of nodose arteriosclerosis, show little tendency to undergo atheromatous and calcareous changes, but like other gummatous infiltrations, are prone to undergo cicatrization with the formation of depressed, radiating scars. Microscopically, the changes are of those of a *mesarteritis*, with infiltration of lymphocytes and plasma cells along the vasa vasorum, a coincident hyperplasia of the intimal tissues, gradual degeneration and absorption of the normal elements of the media and of the new inflammatory tissue, and, finally, replacement fibrosis.

**Pathogenesis.**—The pathogenesis of arteriosclerosis, except of the syphilitic form, is still obscure. While most authorities agree that the process is primarily of a degenerative character, there is at present no consensus of opinion as to whether the deterioration has its starting point in the media or in the intima.

**Associations and Sequels.**—The frequent association of arteriosclerosis with *chronic nephritis* was first pointed out by Sir George Johnson[1] in 1868 and four years later was emphasized by Gull and Sutton.[2] It is not likely that the two diseases always stand in the same relation with each other.

In the first place, the arteriosclerosis may follow the nephritis in consequence of the retention in the blood of irritants which act either directly on the arterial tissue or indirectly by exciting the vasoconstrictor center, thus causing persistent hypertension; secondly, the arteriosclerosis may precede and induce the nephritis by interfering with the blood supply of the kidneys, thus causing atrophy of the renal substance and replacement fibrosis; thirdly, the two diseases may be coördinate and the result of the same cause.

*Hypertrophy of the heart* is almost constantly present in diffuse arteriosclerosis with hypertension; in other forms of the disease it is frequently absent. According to Hasenfeld[3] and Romberg[4] the hypertrophy occurs only when the thoracic aorta or the splanchnic arteries are extensively involved. Probably in some instances the same cause that produces the arterial disease, also contributes directly to the cardiac hypertrophy, and in others that the cardiac hypertrophy itself by increasing the stress within the vessel leads to or at least intensifies degenerative changes in the aorta. Sclerosis of the coronary arteries or of the aorta at the orifices of these vessels plays an important rôle in the etiology of chronic myocardial disease. When the process develops gradually it usually results in *chronic interstitial myocarditis* or *fatty degeneration of the heart.* Complete obliteration of a large coronary artery by a thrombus, the formation of which is greatly favored by the sclerotic changes, is a common cause of sudden death, the entire cardiac circulation often being instantly interrupted and the heart arrested in fibrillary contractions (Porter[5]). The effect of the thrombosis, when it is not immediately fatal, is the production of an area of anemic necrosis (*myomalacia cordis*), the favorite location of which is the wall of the left ventricle near the apex. The necrotic area may rupture or it may be gradually replaced by a fibroid cicatrix.

[1] Med. Chirurg. Trans., 1868.
[2] Med. Chirurg. Trans., 1872.
[3] Deutsch. Arch. f. klin. Med., Bd. 59, 1897.
[4] Lancet, May 28, 1904.
[5] Jour. of Exp. Med., No. 1, 1896.

Among other consequences of arteriosclerosis, *hemorrhage* is one of the most serious. This accident is most likely to occur when hypertension coexists with the arterial disease. The cerebral and retinal arteries, probably because they are so poorly provided with muscular tissue, are the vessels most frequently involved. Occasionally a sclerotic aorta ruptures without dilating. Ames and Townsend[1] have collected 100 such cases, and in 60 per cent. of these the site of the rupture was just above aortic valves. Another condition dependent upon arterial disease is *aneurysm*. Aortic aneurysms are in the large majority of cases the result of a syphilitic mesarteritis.

Roughening of the intima favors the deposit of *thrombi*, portions of which may be dislodged and carried to smaller vessels as *emboli*. The plugging of small arterial twigs in the substance of the organs, in consequence of thrombosis, embolism, or excessive hyperplasia of the intima, usually leads to a replacement of the more highly specialized parenchyma with fibrous tissue, while obstruction of large branches results in actual necrosis. Thus, *cirrhosis* of *the viscera, softening* of *the brain*, and *gangrene of extremities* are frequently observed as sequels of arteriosclerosis. Finally, arteriosclerosis by impairing the nutrition of the tissues and lessening their resistance to bacterial invasion favors the occurrence of *infectious processes*, especially lobar pneumonia.

**Symptoms.**—These vary considerably depending as they do upon the type, degree, and localization of the disease. If the blood pressure is not unduly high subjective symptoms may be absent for an indefinite period. This is especially true of senile arteriosclerosis. In many cases the first symptoms to attract attention are a gradual deterioration of the general health and a peculiar pallor of the skin, due probably to contraction of the cutaneous vessels rather than to actual anemia. In some cases the impairment of energy is so pronounced that the condition is mistaken for primary neurasthenia.

When the disease is sufficiently advanced, the accessible arteries are found to be prominent, tortuous, and hard. The rigidity of the vessel does not entirely disappear when the pulse is obliterated with the finger, which is evidence that it is not due to the pressure of the blood within, but to changes in the arterial wall. In this connection it should be borne in mind that occasionally there is pronounced hardening of the accessible arteries without the slightest sclerosis of the deeper ones; and, on the other hand, that the accessible vessels may be comparatively soft, when the deeper ones are markedly degenerated.

In diffuse arteriosclerosis the result of nephritis or other causes pronounced hypertension is the rule, but in other forms of the disease the blood pressure is frequently normal or only slightly raised, and it may be lower than normal. Evidences of hypertrophy of the heart, especially of the left ventricle, appear sooner or later in cases with hypertension. In uncomplicated nodular or sensile sclerosis, however, cardiac hypertrophy is uncommon. Accentuation of the second aortic sound is a frequent auscultatory finding in cases with high blood pressure and in those in which the ascending aorta is especially affected. If the aorta is roughened or dilated a systolic murmur may also be heard in the aortic area.

*Cardiac Phenomena.*—Involvement of the coronary arteries results sooner or later in symptoms of myocardial insufficiency, such as dyspnea on exertion, a sense of oppression in the precordium, and various forms of arrhythmia. In the course of time attacks of angina pectoris or of so-called cardiac asthma may also occur, and eventually, as a consequence of cardiac dilatation, there may be signs of relative mitral insufficiency with edema of the legs and symptoms of visceral congestion.

[1] Maryland Med. Jour., July 3, 1897.

*Renal Phenomena.*—In the large majority of cases of advanced arteriosclerosis the urine shows traces of albumin and a few hyaline casts. If the lesions in the kidneys advance to the stage of well defined chronic interstitial nephritis a moderate degree of polyuria supervenes, with the specific gravity of the urine low, but not so definitely fixed as in chronic glomerulonephritis. Functional tests of the kidneys do not usually indicate any marked reduction in the excretory efficiency of the organs. On the other hand, in the cases in which the renal lesions are primary and the arterial changes are secondary, the symptoms of the nephritis (fixation of the specific gravity of the urine, digestive disturbances, cachexia, and tendency to albuminuric retinitis and to uremia) usually stand out conspicuously, while those of the arteriosclerosis are subordinate.

*Nervous Phenomena.*—Various symptoms referable to the cerebrum frequently develop in persons with arteriosclerosis. In some cases these are due to structural changes in the kidneys or heart secondary to the arterial disease or to accidental conditions in no way related to the vascular lesions, but in many instances they may be properly attributed to the arteriosclerosis itself. The most common of these symptoms are sleeplessness, headache, vertigo, tinnitus aurium, mental irritability or depression, and impairment of memory. In some cases recurring attacks of transitory monoplegia or hemiplegia or of aphasia, possibly due to arterial spasm, are a conspicuous feature. More or less persistent hemiplegia or aphasia, the result of actual rupture or thrombosis of a diseased cerebral artery, may also occur at almost any period of the disease. Rarely, arteriosclerotic patients suffer from typical epileptiform seizures or stuporous states, which are apparently not due to complete vascular occlusion by thrombosis or embolism, to heart-block and the Adams-Stokes syndrome, or to uremia, but to the vascular changes themselves. Not infrequently the successive obliteration of minute arterial branches in the brain results in multiple foci of encephalomalacia or cerebral "softening," with emotional instability, episodes of confusion, progressive failure of the mental functions and finally complete dementia.

Occasionally, the vessels of the spinal cord are involved to a marked degree, and when this is the case a secondary sclerosis of the conducting tracts may ensue, producing spastic paraparesis, reflex exaggeration, numbness of the limbs and disturbances of the bladder and rectum (Déjérine).[1] Sclerosis of the peripheral vessels is at times attended by distressing sensory disturbances. These may be simple parasthesiæ—numbness, tingling, etc.; painful cramps of the calves, chiefly at night; or paroxysms of pain with halting and signs of local asphyxia, especially when the muscles are put in motion. This last syndrome, which is known as *intermittent claudication*,[2] *dysbasia angiosclerotica* (Erb), and *angina cruris* (Walton and Paul), was first described as a disease of the horse by Bouley[3] in 1831. Typical cases in man are easy of recognition; the patient while walking experiences pains in the legs or feet, coldness, fatigue, and increasing difficulty in locomotion. Associated with these phenomena there is a lack of pulsation in the dorsalis pedis or posterior tibial, or both. After a short rest all of the symptoms disappear. In rare instances chronic neuritis, usually multiple but occasionally localized, appears to be due to arteriosclerosis. Foerster,[4] has reported a number of cases.

[1] Rev. Neurologique, 1906, No. 8.
[2] Charcot. compt. rend. et mém. de la Soc. de Biol., 1858, 2 ième serie, v.
[3] Arch. gén. de Méd., 1831, xxvii, p. 425.
[4] Wien. med. Woch., Jan. 25, 1913.

*Ocular Phenomena.*—An early diagnosis of arteriosclerosis is often made possible by ophthalmoscopic examination. Important signs are undue tortuosity of the vessels, marked irregularity in their caliber, an abnormal light reflection in the form of a glistening streak along the center of the arterial wall ("silver wire" appearance), indentations of the veins by the arteries at points of crossing, hemorrhages into the retina, and, late in the disease, retinal exudation (arteriosclerotic retinitis) in the form of white dots, which, as a rule, are smaller and more scattered than the white "snowbank" patches of renal retinitis.

*Abdominal Phenomena.*—In rare instances sclerosis of the mesenteric or intestinal arteries is productive of recurring crises of pain in the abdomen similar in many respects to those occurring in the chest in ordinary angina pectoris. This condition has been given a variety of names, although it is usually known by that of *angina abdominis*, which was first used by Bacelli. The attacks occur, as a rule, independently of the ingestion of food, and are more likely to develop when the patient reclines than those of angina pectoris. Besides the pain there are usually several other features, including paroxysmal hypertension of the pulse and transient paresis of the segment of bowel involved, with tympanites and constipation. Vomiting may also occur, and in some cases the abdomen is so sensitive during the seizure that the weight of bedclothing is unbearable. The close resemblance of the syndrome to various other painful conditions involving the gastro-intestinal tract, such as peptic ulcer, acute intestinal obstruction, pancreatitis, muco-membranous colitis, etc. is worthy of emphasis. Differentiation is difficult, but it is possible when the manifestations of arteriosclerosis elsewhere give the clue and the attacks are relieved by remedies directed against the arterial condition, such as nitrites and iodids.

Acute obstruction (paralytic) of the bowel, due to thrombotic occlusion of sclerotic mesenteric arteries, is rarely observed. The symptoms of this condition develop very suddenly and consist of severe pain, abdominal distention, hematemesis or enterorrhagia, and collapse. Occasionally uncomplicated hematemesis or enterorrhagia may be traced to the spontaneous rupture of a sclerotic gastric or intestinal vessel.

A slight degree of hepatic cirrhosis is sometimes attributable to general arteriosclerosis, and Hoppe-Seyler, Fleiner and Opie have described cases of chronic interstitial pancreatitis which were apparently due to the same cause. In Opie's case the pancreatic lesion was accompanied by diabetes.

**Prognosis.**—This depends upon the nature, degree and localization of the vascular changes. While the process, or at least its manifestations, may sometimes be held in check by appropriate treatment, and while many persons in whom it has developed at a comparatively early period live to advanced age, nevertheless, it is always dangerous on account of the possibility of cerebral apoplexy, cardiac failure, angina pectoris, etc. The presence of high blood pressure, of pronounced cardiac hypertrophy or of chronic nephritis makes the outlook distinctly more grave, and that of retinal hemorrhage or of progressive weakness and emaciation, highly unfavorable.

**Treatment.**—The chief indications are to remove, if possible, the causes which have led to the disease and to keep the blood pressure within bounds. The regulation of the diet is very important. Stimulating foods must be interdicted. Generally speaking, a diet that is relatively rich in vegetables and cereals is best suited. Even more important than the quality of food, however, is the quantity. As Mitchell Bruce has said, the chief maxim of the dietary is not to avoid this or to eat that but to observe strict moderation in all things. Alcoholic beverages should be prohibited and tobacco used spar-

ingly, if at all. As far as is possible the patient should be protected from all unnecessary excitement. A course of treatment at one of the well-known spas or even a change of scene often exercises a beneficial influence upon the disease, and doubtless largely by securing mental tranquility. All physical over-exertion must be rigidly avoided, although moderate systematic exercise in the open air should be encouraged, unless the blood pressure is excessively high or there are manifestations of cardiac insufficiency. When active exercise is contraindicated gentle massage may prove of service.

Drugs, as a rule, play only a secondary part in the treatment. In syphilitic arterial disease, especially aortitis, arsphenamin should be given cautiously and in small doses, and followed by mercury and iodids. Even in the absence of syphilis, iodids, if given in moderate doses and for a considerable period, sometimes seem to do good in the premature forms of the disease. Perhaps no single measure, is so uniformly beneficial, however, as the periodic use of a pill of blue mass at bedtime, followed by a saline cathartic in the morning.

High blood pressure is best controlled, as a rule, by dietetic and hygienic measures, nitroglycerin and other powerful vasodilators being reserved for such emergencies as dyspneal or anginal attacks. Excessive arterial hypertension may require absolute rest, a spare diet, preferably of milk, free catharsis and blood-letting. Bromids, if given in moderate doses and at bed-time, are often useful in allaying nervous irritability and promoting sleep. When symptoms of cardiac insufficiency appear the treatment becomes that of chronic myocarditis (see p. 651).

## AORTITIS

Aortitis, except as a part of general arteriosclerosis, has not received much attention, although it is a comparatively common condition. In the large majority of cases it is a result of syphilis, but in some instances it is due to rheumatic fever, and it may occur as a complication of septicemia, typhoid fever or any one of the acute infectious diseases. The occurrence of acute aortitis is favored by the presence of chronic aortic lesions. Syphilitic aortitis is found in from 4 to 7 per cent. of all hospital necropsies, and in at least three-fourths of all bodies showing other well-marked evidences of acquired syphilis. The interval between the time of the syphilitic infection and the occurrence of aortitis varies from a few months to thirty years, usually it is from three to five years.

**Morbid Anatomy.**—In non-luetic acute aortitis the aorta may show very little gross change, unless the process is a severe one, and then the vessel is often more or less dilated, its inner surface injected and beset with rose-colored or opalescent patches of varying size. Microscopically, all three coats of the artery may be affected, but the conspicuous lesions are found in the media and consist of an edematous exudation, a cellular infiltration of lymphoid and plasma cells, and a considerable destruction of elastic fibers and muscle elements, especially in the vicinity of the vasa vasorum.

Eventually, as the process becomes chronic, the cellular infiltration gives place to a reparative fibrosis. The changes of syphilitic aortitis are described under the heading "Arteriosclerosis" (see p. 711).

In both simple and luetic aortitis the thoracic aorta, especially the arch, usually bears the brunt of the damage, probably, as Klotz[1] points out, because of the rich lymphatic supply of this portion of the vessel.

[1] Jour. Amer. Med. Assoc., June 23, 1917.

**Symptoms.**—The most constant symptoms are pain in the chest and dyspnea. The pain is referred to the upper sternum or beneath it and may be merely a sense of oppression or of a true anginal character, radiating to the shoulder and arm of either side. A harsh, unproductive cough is not uncommon, and in some cases, especially of syphilitic aortitis, fever of an irregular type is also present. According to Broadbent[1] the occurrence of anginal attacks in a patient with a febrile temperature is very suggestive of acute aortitis.

**Physical Signs.**—Inspection often reveals throbbing of the carotids and pulsation in the suprasternal notch. A thrill or shock, usually diastolic, is sometimes palpable. On percussion an area of dulness may be found above the heart, in the region of the aortic arch. Of the auscultatory indications the most important is a loud aortic second sound of a peculiar metallic or bell-like quality. If the aortic valves are also implicated or if the disease has already resulted in dilatation of the aortic ring a murmur, diastolic or systolic, or double, may be audible in the aortic area. X-ray examination frequently shows enlargement and increased density of the aortic shadow. The blood pressure is not often increased; indeed, in the chronic cases it is usually low.

The symptoms and signs of chronic aortitis are similar to those of acute aortitis; fever, however, is never observed, and evidences of aortic valvular disease, especially aortic insufficiency, are frequently conspicuous.

**Diagnosis.**—The most reliable indications of aortitis are a causal factor, the occurrence of pain in the region of the upper sternum, increased supracardiac dulness, the presence of a loud bell-like second sound or of a diastolic murmur, and enlargement of the aortic shadow. *Aortic aneurysm* may be difficult to exclude, although in this condition there is frequently a distinct protrusion of the chest-wall with a characteristic heaving pulsation. The area of dulness and the aortic shadow are usually more irregular in outline than in aortitis, and pressure symptoms are, as a rule, more in evidence.

**Prognosis.**—Aortitis is a serious condition, frequently resulting in incompetence of the aortic valve, aortic aneurysm, or occlusion of the coronary arteries and myocardial insufficiency. Occasionally, it leads to spontaneous rupture of the aorta. An arrest of the disease is all that is to be expected from treatment.

**Treatment.**—Rest, relative or absolute, according to the severity of the symptoms, is essential. Potassium iodid is useful, but in syphilitic cases neither potassium iodid nor mercury should be employed to the exclusion of arsphenamin in doses of 2 gr. (0.1 gm.) gradually increased to 7 gr. (0.45 gm.). For pain nitrites are often efficacious, although morphin is sometimes necessary. The treatment of chronic aortitis is that of general arteriosclerosis (see p. 714).

## THROMBOSIS AND EMBOLISM OF THE ABDOMINAL AORTA

Obstruction of the abdominal aorta by the formation of a thrombus or the lodgment of embolus is comparatively rare. Thrombosis is usually the result of arteriosclerosis, and embolism is, as a rule, secondary to endocarditis, chiefly mitral stenosis. Occasionally, however, an embolus has its origin in an aneurysm of the thoracic aorta.

**Symptoms.**—The onset may be sudden or gradual. The usual indications are pain in the abdomen and in the lumbar region radiating to the limbs, disturbances of micturition, absence of pulsation in the vessels of the legs,

[1] Broadbent: Heart Disease, New, York, 1900.

and coldness and pallor of the skin of the legs, followed by lividity, numbness, paresis and finally gangrene.

In acute cases the pain may be agonizing and accompanied by profound shock. If the obstruction is at the bifurcation of the aorta abdominal pain and vesical disturbances may be absent.

The **prognosis** is exceedingly grave. Death may occur within twenty-four hours or after the lapse of two or three weeks. According to Hesse[1] an attempt was made to remove the obstruction in 10 of the 73 cases on record and was successful in 5. He advocates transperitoneal aortotomy in recent cases of embolus and high amputation of the thigh in thrombosis.

## PERIARTERITIS NODOSA

This rare disease was first accurately described by Kussmaul and Meyer[2] in 1866. Only about 42 proved cases are on record (Manges and Bæhr[3]). Anatomically, the characteristic feature is the occurrence of small nodular swellings, about the size of a pea or less, on many of the small and medium-sized arteries. The nodules are localized inflammatory lesions, which eventually involve all the coats of the vessel and frequently give rise to true aneurysmal dilatations. The arteries of the stomach and bowel, kidneys, liver, spleen, heart, voluntary muscles and subcutaneous tissues seem to be the vessels most often attacked, while those of the lungs and brain usually escape. The disease is an acute inflammatory process, which apparently involves first the adventitia of the artery and the perivascular lymphatics, but soon extends to all the coats of the vessel and eventually results in absorption of the elastica, in degeneration of the muscular fibers of the media, with secondary fibrosis, and in compensatory thickening of the intima. Consequent upon narrowing or thrombotic occlusion of the affected vessels, secondary changes of a necrotic or degenerative character occur in the various organs. Other lesions, such as glomerulonephritis, may also appear as an effect of the primary inciting agent.

Periarteritis nodosa is probably of infectious origin, but nothing definite is known in regard to its **etiology.** Syphilis has been suspected, but spirochetes have never been found in the lesions. The disease shows a decided predilection for males and occurs chiefly in adult life. A history of tonsillitis is reported in many of the cases.

The **symptoms** vary greatly in different cases. More or less severe abdominal pain of a cramp-like character is rarely absent, and accompanying it there may be vomiting and diarrhea. In a number of cases the disease has been mistaken for appendicitis, cholecystitis, pyelonephritis or perforative peritonitis. Pain in the voluntary muscles and along the peripheral nerves, sometimes with sensory changes and slight paresis, may be an early feature and suggest polyneuritis, polymyositis, or even trichinosis. Pain in the joints is also common. An erythematous, purpuric, or maculopapular rash is sometimes observed. Albuminuria, hematuria, local or general edema and other evidences of nephritis are fairly constant manifestations and may occur early in the disease. Moderate fever and a pronounced polymorphonuclear leucocytosis are almost always present. The most suggestive phenomenon is the occurrence of nodules in the subcutaneous tissues, and the diagnosis during life has rarely, if ever, been made without them. They

[1] Archiv. f. klin. Chirurg., 1921, No. 4, 812.
[2] Deutsch. med. Woch., 1866, i, 484.
[3] Amer. Jour. Med. Sci., Aug., 1921.

appear in about 25 per cent. of the cases and are usually painless and without pulsation. Symptoms referable to the heart, such as dyspnea, palpitation and syncopal attacks, have been conspicuous features in a few instances. Slight jaundice has been noted by Graf, Versé and Benedict. The lungs and brain are usually spared, although the case reported by Chvostek[1] was mistaken for one of encephalitis and the cases reported by Fletcher[2] and by Dickson[3] were thought to be meningitis.

The disease usually ends fatally within a few weeks or months, although remissions sometimes occur and in this case the course may be protracted over a period of a year or more. Death may be due to uremia, cardiac insufficiency or, as in Klotz's[4] two cases, hemorrhage caused by ruptured aneurysmal sacs.

## MULTIPLE HEREDITARY TELANGIECTASES

In 1901 Osler[5] described a "family form of recurring epistaxis with multiple telangiectases of the skin and mucous membranes." In 1907 he collected from the literature and from his own experience eight families affected with the disease[6] and since 1907 a number of additional cases have been reported by other writers. In the family cited by Hutchinson and Oliver[7] three successive generations were affected. In the family reported by Audry[8] there were 15 cases in 4 generations.

The disease is essentially familial and hereditary; it is transmitted by males as well as females; it affects the two sexes about equally; and it shows little atavistic tendency.

The telangiectases, which vary in size from a pinpoint to a pea, occur chiefly on the mucous membranes of the nose and mouth, but they may develop on the face, arms, hands and other parts of the body. Epistaxis is a characteristic feature. The attacks may begin in early childhood and recur through life. Less frequently there is also bleeding from the mouth, or, as a result of trauma, from cutaneous telangiectases. Bleeding from cuts of the skin is never excessive. The blood coagulation time is normal. The pathogenesis of the disease is unknown.

Much confusion exists in the classification of telangiectatic lesions of the skin and mucous membranes, but, as a rule, this condition may be distinguished from angioma serpiginosum of Hutchinson,[9] from purpura annularis telangiectodes of Majocchi[10] and from so-called essential or primary telangiectases, by its hereditary and familial nature, its predilection for the mucous membranes, and its tendency to cause hemorrhage, especially epistaxis.

**Treatment.**—Telangiectases in accessible regions are best destroyed by the electric-needle process. Epistaxis may be checked by styptic lotions or applications of epinephrin, but plugging the nostrils is frequently necessary.

[1] Allg. Wien. Med. Zeit., 1877, No. 28.
[2] Ziegler's Beitrage, 1892, xi.
[3] Jour. of Path. and Bact., 1907, xii.
[4] Jour. Med. Research, 1917, xxxii, 1.
[5] Johns Hopkins Hosp. Bull., 1901, xii, 333.
[6] Johns Hopkins Hosp. Bull., 1907, xviii, 402.
[7] Quart. Jour. of Med., 1916, ix, 67.
[8] Lyon Médical, 1920, xi, 469.
[9] Arch. of Surg., 1889–90 and 1890–91.
[10] R. Acad. delle Scien. dell'Institut. di Bologna, 1905.

## THROMBO-ANGIITIS OBLITERANS

This is a progressive inflammatory condition of the arteries and veins, of the extremities, especially of the legs, resulting in consecutive thrombosis, organization of the clot, and conversion of the affected vessel into a fibrous cord, and terminating in gangrene of the part. Although its etiology is obscure, the disease is probably of an infectious or toxic nature. In this country it is confined almost exclusively to Russian or Polish Jews, and occurs chiefly in males between the ages of 20 and 40. The excessive use of tobacco and hereditary instability of the sympathetic nervous system are believed to exercise an important etiologic influence. According to Buerger,[1] whose studies have thrown much light upon the pathology of the disease, the changes in chronologic order are: (1) an acute inflammatory lesion with occlusive thrombosis, the formation of miliary giant-cell foci; (2) the stage of organization or healing, with the disappearance of the giant-cell foci, the organization and canalization of the clot, the disappearance of the inflammatory products; (3) the development of fibrotic tissue in the adventitia that binds together the artery, vein, and nerves.

**Symptoms.**—The disease usually begins in one of the legs and only exceptionally involves the upper extremities. The important features are (1) pain, especially when the foot is held down, or intermittent claudication (see p. 713), often preceding the development of trophic changes for months or years; (2) disappearance of the pulses, especially in the dorsalis pedis, posterior tibial and popliteal arteries, more rarely in the radial and ulnar arteries; (3) blanching of the limb in the elevated position and reddening of it in the pendent position; (4) migrating phlebitis of certain superficial veins, particularly the external or internal saphenous; and finally (5) gangrene of the toes or of the whole foot or leg, rarely of the fingers or hand. Transitory vasomotor phenomena, such as alternate redness and pallor, occurring independently of position, and various superficial trophic disturbances, such as bullæ, ulcers, atrophy of the skin and impaired nail growth, also occur in some cases.

**Diagnosis.**—Raynaud's disease and erythromelalgia are the conditions most likely to be confused with thrombo-angiitis obliterans. In *Raynaud's disease* the local syncope develops suddenly and usually simultaneously in symmetrical parts; there is no history of antecedent pains; the fingers are much more frequently affected than the toes; the associated vasomotor and sensory phenomena are intermittent and more distinctly dependent upon variations in temperature than those of thrombo-angiitis obliterans; and there is no actual loss of the pulse in the vessels of the affected limbs. In *erythromelalgia*, although pain and redness are especially marked when the affected member hangs down, the symptoms are aggravated by warmth and relieved by cold, the skin feels hot to the hand, the arteries throb, and there is no tendency to gangrene.

**Treatment.**—The disease is a progressive one and in the large majority of cases treatment has been only palliative or of temporary benefit. The following measures have been employed singly or in succession: Applications of superheated air, the induction of passive hyperemia by Bier's suction method, the systematic use of substances to lessen the viscosity of the blood, as Ringer's solution subcutaneously or a 2 per cent. solution of sodium citrate intravenously, ligation of the femoral vein, and arteriovenous anastomosis. Steel[2] has reported several cases

[1] Amer. Jour. Med. Sci., 1917, cliv, No. 3.
[2] Jour. Amer. Med. Assoc., Feb. 12, 1921.

in which the collateral circulation was successfully re-established by intravenous injections of sodium citrate, in conjunction with hot-air baths and the oral administration of potassium iodid. His technic is as follows: During the first month the patient is kept in bed with the legs constantly under a hot air electric light bath at 110° F.; 250 c.c. of 2 per cent. sodium citrate solution is given intravenously every second day. The second month the interval of injection is lengthened to every third or fourth day; daily leg massage is given, and the patient is put in a wheel chair with the feet hanging down a short time each day; or, if the case is not advanced, some walking is allowed. The intervals of injection are now gradually lengthened until at the end of a year the patient gets one every two weeks. Increased walking is permitted as the symptoms subside and evidence of a functional collateral circulation appear. Potassium iodid, 10 grains (0.6 gm.) three times daily, is given during the whole course of treatment.

## ANEURYSM

An aneurysm is a more or less circumscribed dilatation of an artery. If the dilatation involves the whole contour of the vessel it is known as a *fusiform aneurysm.* If the dilatation is like a pouch, involving only a portion of the arterial circumference and communicating with the lumen of the vessel by a relatively small orifice, it is termed a *saccular aneurysm.* Incomplete rupture of the artery from within, with the passage of the blood for a greater or less distance between the tunics, constitutes a *dissecting aneurysm.* The latter is observed chiefly in the aorta. A preternatural communication between an artery and a contiguous vein, a result of ulceration or of a wound, is known as an *arteriovenous aneurysm* or, if the communication is indirect through an interposed aneurysmal sac, as an *aneurysmal varix.* An encapsulated hematoma produced by the rupture of a diseased or healthy artery and remaining in open communication with the blood-stream is described as a *false aneurysm.*

**Etiology.**—Aneurysms are due to a loss of elasticity or a lack of resistance in the arterial wall. In the vast majority of cases this condition is a result of arteriosclerosis. Syphilitic sclerosis (mesarteritis) plays a preponderating rôle, definite evidence of syphilis being obtainable in at least three-fourths of all cases. "It is sufficiently near the truth to say that women never have aneurysm except they have had syphilis" (Goodhart). Ordinary senile atheroma is a very unusual cause. Occasionally, infections other than syphilis, such as rheumatic fever and septicemia, excite a mesarteritis, which subsequently leads to aneurysm. In the smaller arteries dilatation sometimes follows an eroding process which has invaded the wall of the vessel from without. Embolism is another cause of the disease in smaller vessels. If the embolus is calcareous it may act by mechanically injurying the artery; if it is infective, it may act by exciting inflammatory lesions in the arterial wall. The occurrence of multiple, "mycotic," aneurysms in the course of subacute infective endocarditis is not very uncommon. In rare instances aneurysm is traceable to a slight cut or puncture of a healthy artery or to a violent blow that has lacerated the intima.

The immediate cause of aneurysmal dilatation in persons with chronic arterial disease is frequently sudden physical exertion, as in lifting heavy weights, mounting steep ascents, straining at stool, etc. Age, sex, and

occupation are general etiologic factors of considerable importance. While aneurysm may occur at any age, the period of maximum liability, is that of greatest physical activity, or between the ages of 35 and 55. Of 880 cases collected indiscriminately by Hare and Holder[1] 350 occurred between the ages of 35 and 45 years, 204 between the ages of 45 and 55 years, and 188 between the ages of 25 and 35 years. Le Boutillier[2] has collected 60 cases in subjects under 20 years of age. Of these, 14 were under 12 years, and 18 involved the thoracic aorta and 5 the abdominal aorta. Phanomenow's case[3] was in a fetus of 8 months. The disease is four or five times more common in men than in women. Persons engaged in laborious occupations are much more prone to it than others whose work is light. Negroes suffer in greater proportion than white men and among negroes the preponderance of the male sex is somewhat less pronounced.

The incidence of aneurysm varies in different countries, and the figures are, of course, higher for hospitals than for the entire community. Müller[4] among 10,360 necropsies at Jena found 183 aneurysms (1 in 57); at Guy's Hospital,[5] London, among 18,678 necropsies there were 325 aneurysms (1 in 57); at Johns Hopkins Hospital,[6] Baltimore, among 3100 necropsies there were 99 aneurysms (1 in 31); and at Charity Hospital, New Orleans, Lemann[7] found among 2000 necropsies, 67 aneurysms of the aorta (1 in 30), and at the Massachusetts General Hospital among 3500 necropsies there were 53 aneurysms (1 in 66), 40 being aortic.[8]

**Location.**—The aorta is by far the most common site of aneurysm. According to Oswald Browne,[9] of 631 cases of aneurysm treated at St. Bartholomew's Hospital, London, between 1867 and 1897 the aorta was affected in 468 (74 per cent.). Of 332 cases of aneurysm other than aortic, analyzed by Agnew[10] 145 were popliteal, 88 femoral, 21 carotid, 15 axillary, 13 innominate, 12 brachial, 12 subclavian, 9 intraorbital, 3 temporal, 3 gluteal, and 1 subscapular.

**Morbid Anatomy.**—Aneurysms vary considerably in size; those springing from small arteries, such as the cerebral, may be almost microscopic, while those arising from the aorta may attain the dimensions of a child's head. In small fusiform dilatations all three coats of the vessel are sometimes demonstrable, but in the larger saccular aneurysms there is often no trace of the media, the wall comprising only the intima and adventitia, both of which, however, are more or less thickened. In many cases areas of atheromatous degeneration are found in the intima. As the aneurysm extends, surrounding tissues become involved in it and eventually participate in the formation of an adventitious fibrous wall, the proper tunics of the vessel at the same time disappearing to a greater or less extent. The lining of a saccular aneurysm is usually covered with a thrombotic deposit, and occasionally this is so extensive that the cavity is virtually obliterated. The oldest layers of clot are attached to the intima and are pale, dry, and often laminated, while the most recent layers are nearest the blood-stream and are dark and soft. Fusiform aneurysms remain, as a rule, perfectly free from clot.

[1] Amer. Jour. Med. Sci., Oct., 1899.
[2] Amer. Jour. Med. Sci., May, 1903.
[3] Arch. f. Gynäkol., 1881, xlviii.
[4] Zur Statistik der Aneurysmen, 1902, Jena.
[5] Osler, quoted from Bryant, Brit. Med. Jour., Nov. 27, 1909.
[6] Osler, Schorstein Lectures, Brit. Med. Jour., Nov. 27, 1909.
[7] Amer. Jour. Med. Sci., Aug., 1916.
[8] Marble and White, Jour. Amer. Med. Assoc., July 26, 1920.
[9] Aneurysm of the Aorta, 1897.
[10] Principles and Practice of Surgery, 1878, vol. i, 546.

## ANEURYSMS OF THE THORACIC AORTA

Of aneurysms of the thoracic aorta, about one-half involve the arch about one-third the ascending aorta, and about one-sixth the descending aorta. Not rarely several aneurysms are present at different points. In a series of 265 aneurysms of the aorta or its principal branches, Lucke and Rea[1] found that about 20 per cent. were multiple. The saccular form of aneurysm is most commonly observed. The size varies from that of a pea to that of a cocoanut.

**Results.**—As the aneurysm increases in size it either displaces the adjacent viscera or compresses them. Some of the effects of pressure are purely mechanic, others are of an inflammatory or microbic nature. Hypertrophy of the left ventricle is present in many cases, but it is probably a result of arteriosclerosis or of associated valvular disease, rather than of the aneurysm itself. Occasionally an aneurysm of the ascending aorta by dilating the aortic ring brings about relative aortic insufficiency. Death from asphyxia is not rare, especially in aneurysms of the transverse arch. Compression of one of the main bronchi, usually the right, is of frequent occurrence. It may result primarily in overdistention of the affected lung and ultimately in bronchiectasis with fibrosis of the lung, in atelectasis, or in pneumonia with suppuration or gangrene. Erosion of the vertebræ, sternum or ribs occurs in many instances. Occasionally, an aneurysm of the descending aorta lays open the spinal canal and involves the cord.

The most common termination of thoracic aneurysm is by rupture, death resulting from this cause in about 50 per cent. of all cases. It is more frequent in aneurysms of the desending arch and decending aorta than in those of the ascending or transverse arch, which indicates that the more freely the sac can develop the more likely it is to burst. The blood may escape into the pericardium, one of the pleuræ bronchi, or lungs, the trachea, the esophagus, the superior vena cava, the pulmonary artery or the posterior mediastinum.

In 1890 Pepper and Griffith[2] collected from the literature 29 cases of perforation into the superior vena cava and 14 others have been added since that date (Herrick[3]). In 1907 Kappis[4] found recorded 32 cases of perforation into the pulmonary artery. External rupture is comparatively rare (3 cases only in 150—O. Browne). While rupture usually proves fatal within a few minutes, life is occasionally maintained, as in the case of the celebrated surgeon Liston,[5] for several weeks or months after the accident. In the cases without rupture death may be due to secondary changes in the lungs, to secondary or concomitant disease of the heart, to asphyxiation from compression of the trachea, to intercurrent disease not directly related to the aneurysm, to exhaustion, or very rarely to embolism of the cerebral vessels. In rare instances thoracic aneurysms remain stationary for many years or even undergo spontaneous cure by thrombosis. Whipham[6] reports a case which was known to have existed for at least 16 years, and Hirsch and Robins[7] report one in which a large thoracic aneurysm remained virtually unaltered for 25 years.

*Aneurysm of the Ascending Aorta.*—This is the portion of the aorta most frequently involved, although not rarely the ascending aorta and transverse

[1] Jour. Amer. Med. Assoc., Sept. 17, 1921.
[2] Trans. Assn. Amer. Phys., 1890, v.
[3] Amer. Jour. Med. Sci., Dec., 1919.
[4] Deutsch. Archiv. f. klin. Med., 1907, xc, 5.
[5] Lancet, Dec. 11, 1847.
[6] Brit. Med Jour., Nov. 2, 1901.
[7] Maryland Med. Jour., 1903, xlvi, 93.

arch are involved together. In the large majority of cases the aneurysm springs from the convex side of the vessel and projects to the right; only rarely does it arise from the concave side and project to the left. The structures most commonly subjected to pressure are the superior vena cava, pulmonary artery, and left recurrent laryngeal nerve. The innominate artery is rarely involved. Rupture into the pericardium or into the right pleural cavity is particularly frequent.

*Aneurysm of the Transverse Arch.*—The aneurysm may extend directly backward, or toward the surface, to the right and upward. The innominate artery is sometimes involved. The structures most frequently compressed are the trachea, sternum, left bronchus, esophagus, and left recurrent laryngeal nerve. Death by asphyxia due to pressure upon the trachea is not uncommon. When rupture occurs it is usually into the left pleural cavity, left bronchus, trachea, or pericardium.

*Aneurysm of the Descending Arch.*—An aneurysm in this location usually extends to the left and backward, presenting in the left interscapular region close to the spine. The dorsal vertebræ and ribs are frequently eroded. Other structures likely to be compressed are the esophagus, left bronchus and trachea. The majority of cases terminate by rupture, which usually takes place into the left pleural cavity, left bronchus or esophagus.

*Aneurysm of the Descending Aorta.*—The usual site is a few inches above the diaphragm. The lower dorsal vertebræ are often eroded. The larger number of cases end in rupture, which is most frequently into the left pleural cavity or the esophagus.

**Symptoms.**—In typical cases aortic aneurysm is revealed by characteristic symptoms and physical signs. Not infrequently, however, one of these forms of evidence is wholly wanting, and sometimes the disease gives no indication whatever of its existence during life, unless it be at the close when a fatal rupture occurs. Latency is particularly common in aneurysms of the descending aorta. Broadbent has divided thoracic aneurysms into two classes, namely *aneurysms of physical signs* and *aneurysms of symptoms*, from the predominance of physical signs and symptoms respectively, the former term applying to aneurysms of the ascending aorta and first part of the arch, the latter to aneurysms of the transverse and descending portions of the arch.

*Pain in the Chest.*—This is one of the most constant symptoms. It varies in intensity from a dull ache to the agony of true angina pectoris. When due to erosion of bones it is usually of boring or gnawing character. It may be paroxysmal or more or less persistent. It is increased by exertion and sometimes by change of posture. In many cases it radiates to the neck and down one of the arms. In aneurysms of the descending thoracic aorta it is often felt in the back or along the intercostal nerves of one side, usually the left. Occasionally an aneurysm reaches enormous dimensions and even erodes the bones without causing any pronounced pain.

*Dyspnea*, although not constant, is an important symptom, and may be due to compression of the trachea or bronchi or nerve-trunks, to pulmonary complications or to hydrothorax. When due to compression of the trachea it is frequently accompanied by inspiratory stridor. Not rarely the dyspnea occurs chiefly at night and is distinctly paroxysmal.

*Cough* is very common. It may be due to pressure upon the trachea, a bronchus, the lung, or the recurrent laryngeal nerve. In many cases it is quite distinctive in being of a hoarse, clanging or "brassy" character. Considerable expectoration may accompany the cough after the bronchi or lungs have become infected.

*Alteration of the Voice.*—In some instances this is the first symptom to

attract attention. As a rule, there is only hoarseness, but occasionally, as a result of paralysis of both vocal cords, there is complete aphonia.

*Hemoptysis.*—Apart from the copious hemorrhage that occurs at death from rupture of the sac, there is often expectoration of blood in small quantities over long periods. Thus, in 100 cases of aortic aneurysm analyzed by H. Batty Shaw[1] hemoptysis is mentioned as a symptom in 19. The cause of the bleeding may be inflammation of the trachea or bronchi, erosion of the lung, or weeping through the aneurysm itself.

*Dysphagia.*—While a slight degree of dysphagia is observed in a considerable percentage of cases, signs of actual obstruction of the esophagus with regurgitation of food are rare, the esophagus being more often pushed to one side by the aneurysm than compressed by it.

**Physical Signs.** *Inspection.*—In many cases careful inspection of the chest in a good light reveals an abnormal area of pulsation, the location of which varies with the part of the aorta involved. In aneurysms of the ascending arch the pulsation is usually to the right of the sternum, in the second or third interspace. Very exceptionally, when the aneurysm springs from the concave side of the vessel, it is to the left of the sternum. In aneurysms of the transverse arch the pulsation is in the episternal notch, over the manubrium, or in the interspaces to the right or left of the manubrium. In aneurysms of the descending arch or aorta the pulsation is usually to the left of the spine, between it and the scapula. Erosion of the dorsal vertebræ occasionally gives rise to kyphosis in this region. With the pulsation there is frequently a distinct circumscribed bulging. Over large protruding aneurysms the skin is sometimes glazed and red. The apex-beat, owing to enlargement of the heart, pressure of the aneurysmal sac, or elongation of the aorta, may be displaced downward and to the left.

Distention of the superficial veins of the neck, chest or arms is a conspicuous sign when one of the large venous trunks is compressed. Marked cyanosis, edema of the head, trunk and upper extremities, injection of the eyes and even exophthalmos may also be observed if the superior vena cava is completely obstructed. Clubbing of the fingers of one hand occasionally supervenes when the impediment to the venous circulation is prolonged. The respiratory movements on one side may be diminished or abolished if a large bronchus is obstructed.

In many cases the pupil on one side is dilated or contracted. This may be due to pressure upon the ciliospinal branches of the sympathetic, irritation causing mydriasis, and paresis, myosis. More frequently, however, anisocoria is probably due, as Wall and Walker have shown, to unequal blood pressure in the carotid and ophthalmic arteries. In a third and comparatively small group of cases the inequality of the pupils is caused by concomitant tabes, both the aneurysm and the tabes being a part of syphilitic infection (Osler). Occasionally flushing and sweating on one side of the face is also observed as a manifestation of sympathetic involvement. Laryngoscopic examination frequently shows one vocal cord, usually the left, to be immobile and in the cadaveric position. In this connection it should be borne in mind that pressure on the recurrent laryngeal nerve may affect for a time only the abductor fibers, in which case there may be no alteration of the voice to attract attention to the laryngeal paralysis.

*Palpation*, especially if bimanual, may reveal a pulsation that is not apparent to the eye. In protruding aneurysms the pulsation is almost always distinctly expansile, whereas any motion that is imparted to a solid tumor in contact with the aorta is merely a forward thrust. The sac

[1] International Clinics, vol. i, 1901.

is soft or firm to the touch according to the amount of clot within it. At the end of each systolic pulsation there is sometimes a strong impact or diastolic shock—a sign almost pathognomonic of aneurysm. It is due to the recoil of blood within the sac. In many cases the pulsation is accompanied by a tactile systolic thrill.

Aneurysms of the thoracic aorta often transmit to the trachea a pulsation which is felt as a distinct downward jerk—a sign first described by Oliver[1] in 1878 and known as the tracheal tug. To elicit it the head should be thrown back, the mouth closed, and the cricoid cartilage grasped between the finger and thumb and pressed upward. Although this phenomenon, which probably depends upon the presence of mediastinal adhesions, may sometimes be felt in tumors of the mediastinum and enlarged bronchial lymph-nodes, it is most frequently found in aneurysm, and therefore it is a valuable corroborative sign. Occasionally a lateral rather than a downward tug is elicited (Cardarelli's sign). Not infrequently the radial pulse on one side is delayed and enfeebled. This may be due to compression of an aortic branch or to partial occlusion of an arterial orifice by thrombus, but in the majority of cases it is probably due to the damping effect of the aneurysmal sac on the pulsations. In large aneurysms with elastic walls, as François-Franck, Flint, Osler and others have shown, the arterial wave may be converted into a continuous stream, and in consequence there may be complete obliteration of the pulse in the abdominal aorta and its branches and even in the peripheral arteries without serious disturbance of the circulation.

*Percussion.*—In many cases an area of dulness, with a sense of increased resistance, is present to the right or to the left of the manubrium, over the sternum, or posteriorly over the dorsal vertebræ or in the left interscapular region. In small and deep seated aneurysms, however, no dulness can be elicited.

*Auscultation.*—In about one-half of all cases auscultation over the aneurysm reveals a blowing systolic murmur or *bruit.* This is caused by a fluid vein which is generated as the blood passes from the aorta into the larger aneurysmal sac. Very often a diastolic murmur is also present. This is usually due to coexisting aortic insufficiency, but in some cases it is apparently due to a backward flow of blood through a narrow orifice into the aorta during diastole. A more important auscultatory sign than these murmurs is a loud ringing second sound synchronous with the diastolic shock.

*X-ray Examination.*—Examination by the roentgen ray affords valuable information and not rarely the diagnosis of aneurysm cannot be made without its aid. Even when the case is not a doubtful one fluoroscopic or radiographic examination is of service in determining the exact position, size and shape of the dilatation, and whether more than one portion of the aorta is involved.

*Communication with the Superior Vena Cava and Pulmonary Artery.*—Rupture of an aortic aneurysm into the superior vena cava is indicated by the rapid appearance of cyanosis, edema, distention of the veins in the upper part of the body, and a humming murmur, which is continuous, but louder in systole than in diastole. Rupture into the pulmonary artery is usually characterized by the sudden occurrence of pain, dyspnea, cough and expectoration, a purring thrill in the pulmonary area, and a continuous rhythmic murmur. Cyanosis is rare. Patients sometimes live for weeks or even months after rupture of the aneurysm into either of these vessels.

[1] Lancet, 1878, vol. ii, 406.

**Diagnosis.**—The diagnosis is easy when there is a distinct area of dulness in the region of the aorta with pulsation, thrill, diastolic shock, bruit, etc., but it may be very difficult if the aneurysm is small and deep seated. An x-ray examination should be made in all cases with obscure thoracic symptoms. Small aneurysms involving the intrapericardial portion of the aorta or springing from the sinuses of Valsava are very likely to be overlooked, because, as a rule, they either remain entirely latent or produce no other symptoms than those of angina pectoris or of aortic insufficiency.

Distinct pulsation in the interspaces near the manubrium or in the episternal notch may occur in insufficiency of the aortic valves, in retraction of the lungs, and in spinal curvature with dislocation of the aorta, but in these conditions the other characteristic signs of aneurysm are absent and pressure symptoms are uncommon. No sharp line of distinction can be drawn between the condition referred to as *simple dilatation of the aorta* and fusiform aneurysm of the aorta, but in typical cases of the former the vessel is merely uniformly dilated, its diameter being 1.2 or 3 cm. above the upper limit of normal (6 cm.), and there is nothing about the enlargement suggestive of a tumor. The condition is usually due to arteriosclerosis or syphilitic aortitis and is often associated with insufficiency of the aortic valves. It gives rise to many of the physical signs and symptoms of aneurysm, but there is never any bulging of the chest wall, the impulse rarely has the heaving quality, usually so characteristic of aneurysm, and severe pressure effects are very uncommon. In the vast majority of cases the diagnosis can be made with certainty by fluoroscopic or radiographic examination.

*Tumors of the mediastinum* sometimes give considerable difficulty, and occasionally even an x-ray examination fails to settle the question. In tumor pulsation, if present, is not expansile, the diastolic shock and ringing second sound are nearly always wanting, and tracheal tug is infrequent. Cachexia, enlargement of the cervical or axillary lymph-nodes, and pronounced dysphagia are points in favor of tumor. On the other hand, a positive Wassermann reaction, evidences of arteriosclerosis, and marked inequality of the two radial pulses are points in favor of aneurysm.

A *pulsating empyema*, if near the heart, may be confused with aneurysm, but the impulse is usually more diffuse than in aneurysm and is rarely expansile. Moreover, empyema is not attended with pressure symptoms nor with the characteristic auscultatory phenomena of aneurysm. The most valuable evidence, however, is furnished by the x-ray. The error of attributing to aneurysm pains due to *primary lesions of the vertebræ* or to *cervical ribs* can be avoided by the timely use of the x-ray in all obscure thoracic conditions.

In *aneurysm of the innominate artery* the pulsating tumor is at the right sternoclavicular articulation, the pulsation in the right radial artery is weak and retarded, the trachea is frequently displaced to the left, and not rarely there is venous congestion and edema over the right side of the neck and right arm, as a result of pressure on the right innominate or the internal jugular vein. *Aneurysm of the pulmonary artery* produces symptoms very similar to those of aortic aneurysm, but it is very rare. A correct diagnosis during life has been made only once or twice. According to Henschen,[1] who has analyzed 34 cases, the most important indications are bulging, pulsation, thrill, pronounced dulness or x-ray shadow, and a loud superficial, rasping, systolic murmur in the region of the second and third left costal cartilages, with intense cyanosis, bloody expectoration, and signs of hypertrophy of the right heart.

[1] Volkmann's Samml. klin. Vorträge. Leipzig, 1906, No. 422, 423.

**Prognosis.**—The outlook is grave. Permanent recovery or a delay in the fatal issue for years is possible, but such a result is rare. The average duration is probably not more than two years.

## ANEURYSM OF THE ABDOMINAL AORTA

Aneurysms of the abdominal aorta are much less common than those of the thoracic aorta, the ratio probably being about 1 in 10. Nixon[1] in 1911 collected 233 cases and in 1918 Marlow and Doubler[2] added 11 more. In Nixon's series only 26 of the patients were females. The usual site is just below the diaphragm in the region of the celiac axis. Erosion of the upper lumbar vertebræ is observed in nearly half of the cases, and in some instances the destruction of bone is so extensive that the spinal cord is encroached upon. The duration of life is not often more than two or three years and the fatal termination is usually brought about by rupture of the sac into the retroperitoneal space or into the peritoneum. More rarely rupture occurs into the bowel, especially the duodenum, into the left pleura or into the inferior vena cava. Spontaneous cure is occasionally observed.

**Symptoms.**—The most constant symptom is pain. This is often of an intense neuralgic character with acute exacerbations. In many cases it radiates from the back around the abdomen or down into the thighs. A continuous boring pain is experienced when the vertebræ are becoming eroded. Vomiting is sometimes a conspicuous symptom. Involvement of the spinal cord gives rise to numbness in the legs and finally to paraplegia. Jaundice has been present in a few instances.

**Physical examination** frequently reveals a pulsating tumor in the epigastrium, somewhat to the left of the median line. The impulse is forcible and, as a rule, distinctly expansile. Sometimes a thrill can also be felt. In about two-thirds of the cases a systolic murmur may be heard over the abdomen or the back. A diastolic murmur is rare. The femoral pulse is frequently retarded and feeble.

**Diagnosis.**—The presence of pulsation, thrill and bruit, singly or together, is not in itself sufficient evidence upon which to base the diagnosis of abdominal aneurysm, as these phenomena are often pronounced in young anemic subjects and in thin neurotic persons, particularly women, in whom the walls of the aorta are perfectly sound. Such *dynamic throbbing of the aorta* may usually be recognized without difficulty by the absence of a definite tumor, expansile pulsation, retarded femoral pulse and all pressure effects. In any doubtful case the x-ray examination must be the deciding test. A *solid tumor* resting upon the aorta sometimes transmits a pulsation which suggests aneurysm. Here again the pulsation is not expansile, but from behind forward; and, moreover, it usually disappears when the patient assumes the knee-elbow position.

**Treatment.**—The treatment of aortic aneurysm is, on the whole, unsatisfactory. The indications are to arrest the destructive luetic process in the arterial wall, to promote clotting within the sac, and to relieve distress. If the case is a recent one and there are no evidences of cardiac insufficiency, courses of arsphenamin and mercury should be employed with the hope of destroying the spirochetes in the vascular tissue. In any case an attempt should be made to reduce the blood-pressure within the aneurysm and thus favor the formation of a clot. For this purpose the treatment suggested by Tufnell[3] may be followed more or less closely, although actual cure cannot be

[1] St. Bartholomew's Hosp. Rep., London, 1912, vol. xlvii.
[2] Amer. Jour. Med. Sci., April, 1918.
[3] Tufnell, Treatment of Internal Aneurism, 1864.

expected from it. The chief elements of the treatment are *rest* and *restriction of diet*. The patient should be kept in bed for a period of from 6 weeks to 3 months, being allowed to get up only to use a commode. Mental excitement of any kind must be avoided. The diet as outlined by Tufnell[1] consists of 2 ounces (60 gms.) of bread and butter, with 2 ounces (60 mils) of milk or tea for breakfast and supper, and 2 or 3 ounces (60–90 gms.) each of bread and meat, with from 2 to 4 ounces (60–120 mils) of milk or claret, for dinner, but it has been found that these amounts of food are inadequate and that a more liberal allowance of solids may be made without detracting in any way from the efficiency of the treatment.

During the period of rest aperients are usually necessary to obviate constipation and the injurious effects of straining in defecation. The employment of gelatin subcutaneously to promote coagulation, as recommended by Lancereaux, was found to be of little value and has virtually been discarded. Potassium iodid, first suggested by Bouillaud, unquestionably relieves pain in many cases, but the manner of its action is not known. It should be given in doses of 10 to 20 grains (0.6–1.3 gms.) thrice daily. The withdrawal of from 15 to 20 ounces (450–600 mils) of blood may be of great service when there is severe pain or dyspnea. Cold applications are also helpful, but in many cases recourse must eventually be had to morphin.

The method of treating aortic aneurysms by means of fine wire introduced through a hollow needle into the sac was first suggested by C. H. Moore,[2] in 1864. Corradi,[3] in 1879, demonstrated that the procedure could be made more effective by passing a galvanic current through the wire, thus producing more rapid and firm coagulation. The operation entails comparatively little risk when performed by an experienced operator and often yields very satisfactory results, almost always relieving pain and in some cases apparently prolonging life. It is only suitable, however, for sacculated aneurysms. The technic of the procedure is briefly as follows: After the skin has been sterilized, an insulated hollow needle or cannula is inserted into the aneurysm where the sac-wall seems nearest to the surface, and through this from 15 to 30 feet (450–900 cm.) of fine platinum-gold wire are introduced from a spool into the sac. The external end of the wire is now connected with the positive pole of a galvanic battery and the current is completed by the application of a large, well-moistened electrode, attached to the negative pole, under the patient's back. Beginning with 5 milliampères, the current is increased by 5 additional milliampères every five minutes until 50 milliampères are reached, and then the current is gradually reduced. At the end of from thirty minutes to an hour the electrodes are disconnected, the needle is withdrawn, the free end of the wire is fixed beneath the skin, and the puncture is sealed. After the operation the patient should remain in bed for a period of two or three weeks so that the clot shall become thoroughly consolidated. An anesthetic is required for aneurysms of the abdominal aorta, as for these the abdomen must be opened, but it is not required for thoracic aneurysms. In 25 cases of the latter reported by Hare there were no accidents and more or less benefit was secured in all. Of 15 cases of abdominal aortic aneurysm, treated by the Moore-Corradi method, analyzed by Matas,[4] 3 patients were apparently cured, 2 were improved, and in 10 the condition was either unimproved or aggravated by the procedure.

[1] Tufnell, Treatment of Internal Aneurism, 1864.
[2] Trans. Med. Chir. Soc., Lond., 1864, xlvii.
[3] La Sperimentale, April, 1879.
[4] Amer. Medicine, June 22, 1901.

## ARTERIAL HYPERTENSION

The arterial blood pressure depends upon the force of the contractions of the left ventricle, the elasticity of the arteries, the peripheral resistance, and to a less extent upon the total volume of the blood, and the viscosity of the blood. The maximum pressure caused by the systole of the ventricle is spoken of as the *systolic pressure;* the pressure at the end of the ventricular diastole, or at the lowest point of the pulse wave, is known as the *diastolic pressure*, and the difference between the two is called the *pulse pressure*. For determining variations in the arterial pressure the sphygmomanometer or sphygmographic tracings must be used, as the finger, even when trained, is unreliable. The systolic pressure measures the working force of the heart. It fluctuates considerably even under physiologic conditions, being influenced by exertion, mental states, sleep, meals, etc. Generally speaking, however, the systolic pressure, as measured in the brachial artery when the individual is at rest, is between 90 and 105 mm. in childhood, between 130 and 140 mm. in middle life, and between 140 and 150 mm. after the sixtieth year. In women the systolic pressure is from 5 to 10 mm. lower than in men.

The diastolic pressure measures the peripheral resistance and is determined largely by the tonus of the arterioles. It is much less subject to temporary fluctuations than the systolic pressure and affords more reliable information than the latter concerning the work required of the heart. It is normally from 25 to 40 mm. lower than the systolic pressure. The pulse pressure measures the variation in pressure in a given artery caused by the heart's contraction and therefore represents the force that is driving the blood to the periphery or the "load" which the heart must carry to maintain the circulation. In the brachial artery it is normally between 30 and 50 mm., but it becomes less and less as the periphery is approached, and in the capillaries it falls to zero, no difference existing in these vessels between the systolic and the diastolic pressure. It may be said in general that at any age a systolic pressure constantly over 150 mm., a diastolic pressure constantly over 100 mm., or a pulse pressure constantly over 50 mm. is pathologic.

Pathologic hypertension, as a more or less temporary condition, may occur (1) in association with certain well recognized intoxications, such as puerperal eclampsia, uremia and lead-poisoning; (2) in association with asphyxia, the result of bronchial asthma, decompensated heart disease, etc., the excess of $CO_2$ causing constriction of the splanchnic vessels by stimulating the vasomotor center; (3) in association with increased intra-cranial pressure, the result of rapidly growing brain tumors, cerebral hemorrhage, etc., the medullary anemia produced in such cases acting as a stimulant to the vasomotor center and causing intense vasoconstriction (Cushing); and (4) in association with various nervous disturbances, such as severe pain, and profound mental or emotional excitement.

*Persistent arterial hypertension* may occur (1) as an expression of chronic glomerular or diffuse nephritis (nephritic hypertension); (2) in association with general arteriosclerosis (arteriosclerotic hypertension); and (3) as a functional condition developing independently of anatomic changes in either the kidneys or the arteries (essential hypertension). The relation of arteriosclerosis to hypertension is obscure. It is certain, however, that extensive disease of the vessels is not incompatible with a normal blood pressure, and equally certain that persistent high blood pressure, irrespective of its cause, is always followed in the course of years by arteriosclerosis. Whether the high blood pressure itself in these cases causes the vascular changes or whether both conditions are the result of some obscure intoxication is not

known. It is usually assumed that arteriosclerosis, especially that form described by Gull and Sutton under the name of arteriocapillary fibrosis, may develop as the primary process and become the direct cause of hypertension, but of this there is no definite proof. It may be that one etiologic factor can produce both conditions, either coincidentally or consecutively.

Arterial hypertension in the course of time is followed by hypertrophy of the heart, and the end-result is usually cardiac failure, cerebral hemorrhage or thrombosis, angina pectoris, acute edema of the lungs, or uremia, the last being usually an expression of primary renal disease, but occasionally a manifestation of secondary vascular nephritis.

## ESSENTIAL ARTERIAL HYPERTENSION

**(Hyperpiesia; Benign Arterial Hypertension; Primary Hypertensive Cardiovascular Disease)**

These terms are used to designate cases in which high blood pressure exists for a longer or shorter period without anatomic changes in either the kidneys or arteries. Such cases were first accurately described by Sir Clifford Allbutt[1] who coined for them the name *hyperpiesia* and defined the condition as one in which high blood pressure is the essential feature and earliest manifestation.

**Etiology.**—The causes of essential hypertension are not definitely known. The condition is more common in men than in women and usually develops in late middle life. In women, as Torrey, Riesman, Hopkins[2] and others have pointed out it often occurs at the time of the menopause. The majority of its victims are persons of apparently robust health and many are overweight. Prolonged mental strain or anxiety, especially if associated with too rich living and deficient muscular exercise, is undoubtedly a potent factor. Tobacco and alcohol may play accessory rôles but are probably not capable in themselves of producing the disease. Syphilis is not a factor. Whether the basic disturbance is a toxemia of metabolic or of intestinal origin, or, as some have supposed, an oversecretion of pressor substance by the adrenals is not clear. Whatever its nature, the site of its operation is probably the arterioles or, as Osler suggested, the working area of the body, between the capillary cells and the lymph spaces.

**Symptoms.**—Essential hypertension may be for a long time latent. The life-insurance examiner in making routine examinations is often the first to discover it. The symptoms for which the patient first seeks advice may be grouped in three classes. In the first class the symptoms are referable to the heart and consist of dyspnea on exertion, palpitation, and precordial discomfort or actual anginal pain. In the second class the earliest manifestations are of neurasthenic character and consist of ready fatigue, lassitude, nervous irritability, disturbed sleep, vague pains in the back and limbs, and varying combinations of the gastric neuroses. In the third class the first indications are chiefly cerebral and consist of dull headache, vertigo, tinnitus aurium, and, perhaps, transient attacks of aphasia or of hemiplegia. Less frequently, the first indication is a slight blurring of vision due to small retinal hemorrhages. Occasionally epileptiform convulsions occur, especially at night, and in this event the diagnosis of uremia is likely to be made.

**Physical examination** often reveals, besides the hypertension, which is often very pronounced (systolic 200–250, diastolic 110–140), accentuation of the aortic second sound and more or less cardiac hypertrophy. For years there may be no obvious changes in the accessible arteries. When full of blood they are usually firm and can be rolled under the finger, but if in a

[1] Med. Chir. Soc., 1903, lxxxvi; Diseases of the Arteries, Including Angina Pectoris; London, 1915

[2] Amer. Jour. Med. Sci., June, 1919.

section of one them the blood is forced out by gentle pressure it will be found that the artery itself is soft. Eventually, however, arteriosclerosis supervenes and in consequence the vessels become thickened and tortuous. Except in the advanced stages of the disease, when secondary changes may have occurred in the kidneys as a result of myocardial insufficiency or of sclerosis of the renal arteries, the urine is usually normal or contains but a trace of albumin and a few hyaline casts. Functional tests indicate no reduction in the efficiency of the kidneys. Ophthalmoscopic examination may reveal nothing abnormal, although in cases of long standing it frequently shows sclerosis of the retinal arteries, retinal hemorrhages, and even arteriosclerotic retinitis (see p. 714).

**Course and Events.**—Essential arterial hypertension is a chronic condition, often lasting over a period of 5, 10, 15 years or longer. In the course of time it is followed by cardiac hypertrophy, arteriosclerosis, and renal fibrosis (vascular nephritis). If recognized early, before the cardiovascular system has undergone any structural changes, it may sometimes be recovered from and in the majority of cases materially aided. Generally speaking, cases of menopausal origin are the most benign. Death may be due to any of the following sequels or complications, arranged in their order of frequency: (1) gradual cardiac insufficiency, (2) cerebral apoplexy, (3) paroxysmal acute pulmonary edema, (4) angina pectoris, (5) intercurrent infection (usually pneumonia); (6) gradually increasing cachexia. In this last condition the cardiac, cerebral and renal symptoms may be unobtrusive, the chief feature being a gradual loss of flesh and strength, with progressive anemia, the patient being confined to bed in some instances for a year or longer before death.

**Diagnosis.**—The differential diagnosis between essential hyperpiesis and chronic glomerulonephritis with arterial hypertension is not usually difficult. Nycturia and polyuria, definite fixation of the specific gravity of the urine at 1010 to 1013, increasing pallor and cachexia, severe headaches with vomiting, impairment of vision, the result not merely of hemorrhages into the retina but of true albuminuric retinitis, and a pronounced reduction of the functional capacity of the kidneys, as shown by the phenolsulphonephthalein and other tests all point to chronic renal disease. A trace of albumin and a few faintly granular casts may be found in the urine in both groups of cases, but generally speaking they are more persistently present in renal hypertension. Patients with essential hyperpiesis who first come under observation after the occurrence of cardiac failure may show as a result of the general venous stasis evidence of serious renal insufficiency, but in such cases there is no history of long-standing nycturia, polyuria and etc.; and the response of the patient to rest and appropriate treatment is often much more prompt and satisfactory than in primary nephritis with secondary hypertension.

**Treatment.**—As arterial hypertension is the result of causes that are not definitely known and seems to be in itself a compensatory process, the chief problem of its management is the protection of the patient from all deleterious influences, especially physical, mental and emotional strain, dietetic excesses, and intercurrent infections. It is not always necessary or advisable for a man of important affairs to give up his business completely, but it is necessary to effect such readjustment in his everyday life that he may secure more opportunities for mental and physical relaxation. When there is a sudden accession of hypertension, when pronounced myocardial symptoms appear, or when there are premonitions of cerebral accidents, rest in bed for a week or ten days is usually imperative. On the other hand, in comparatively robust individuals, with no symptoms referable to the heart or brain, carefully graduated exercise in the fresh air is often decidedly useful. As to the

amount of exercise the functional response of the myocardium must be the determining factor. High blood pressure is no indication of nitrogen retention, and, therefore, if the functional capacity of the kidneys is normal, it is unnecessary to cut out all proteins. It is necessary, however, to lessen materially the total intake of all food, and undoubtedly many patients are better off on diet that is relatively low in proteins. Obese subjects, especially, do well upon a reducing diet. Alcoholic drinks are undoubtedly harmful and so is tobacco in excess, but in many cases 1 or 2 mild cigars a day may do less harm than the discomfort that would result from their withdrawal.

Climate is not without influence. The majority of patients who have symptoms are more uncomfortable in winter than in summer, and therefore a change to a warm climate during the cold weather is desirable, although, of course, it is not always feasible. Turkish baths or other sweating procedures, if not used too frequently, may be of service in patients who are still robust and who show little that is abnormal besides the hypertension. It has not been proved that the condition of the bowels has anything to do with the blood pressure, nevertheless it seems desirable to promote elimination in every way and, therefore, if there is any tendency to constipation, it is advisable to prescribe mild cathartics and to give at intervals of ten days or two weeks a pill of blue mass and a saline.

There is no medicinal treatment for hypertension itself. Potassium iodid is usually recommended, but it is doubtful whether it has any decided influence upon the condition. In climacteric hypertension endocrine therapy, especially the administration of ovarian extract, is sometimes useful in conjunction with rest and bromid medication. Vasodilators, such as nitroglycerin, sodium nitrite, and erythrol tetranitrate are best reserved for emergencies, when the heart or the cerebral vessels give the signal. They are often invaluable when there is embarrassment of the heart, anginoid pain, or unwonted fulness in the head. In vigorous patients with inordinately high blood-pressure venesection, to the extent of 10 to 15 ounces of blood, sometimes, produces very satisfactory results. The d'Arsonval high frequency current often acts favorably, but its effects are, as a rule, transitory. If insomnia calls for active treatment, veronal, a combination of potassium bromid with hydrated chloral, 10 or 15 gr. (0.6–1.0 gm.) of the former with 5 gr. (0.3 gm.) of the latter, will usually be found useful. Patients with definite myocardial insufficiency require absolute rest, careful regulation of diet, and liberal doses of digitalis. Not rarely theobromin will be found a useful adjuvant to digitalis.

## ARTERIAL HYPOTENSION

Much more attention has been paid to high blood pressure than to low blood pressure, probably because the power of the former to produce harmful effects is greater than that of the latter. Indeed, there is no consensus of opinion as to what reading should be regarded as low blood pressure. Arbitrarily, however, one may place the lower limit of systolic pressure in the adult at about 110 mm. Hg. The lower limit of diastolic pressure is even more difficult to place than that of the systolic pressure, as very often the two pressures do not run parallel. Thus, in one case the systolic pressure may be 100 mm. and the diastolic pressure 90 mm. and in another case the systolic pressure may be 90 mm. and the diastolic 55 mm.

Clinically, hypotension is observed as a symptom in the following conditions: (1) Shock, both surgical and anaphylactic; (2) poisoning by certain drugs, such as aconite, chloral, chloroform, alcohol, etc.; (3) acute infections; (4) cachexia from tuberculosis, carcinoma, severe anemia, etc.; (5) certain disorders of internal secretion, as in Addison's disease, myxedema, status lymphaticus, etc.; (6) certain cardiovascular diseases, as in myocarditis and chronic aortitis, unless, as is not rarely the case, the decreased power of the heart is overbalanced by increased resistance in the peripheral circulation; (7) certain nervous disturbances, as in some cases of neurasthenia, paretic dementia, and epilepsy; and (8) certain renal conditions, such as amyloid kidney and cyclic albuminuria.

**Symptoms.**—Persistent hypotension is frequently associated with dull headache, vertigo, lassitude, and ready mental and physical fatigue. Whether these symptoms are an effect of the hypotension, or whether the hypotension is the result of the nervous symptoms, or whether both the nervous phenomena and the low blood pressure are dependent upon a common factor, such as some functional disturbance of the internal secretions, especially adrenal insufficiency, is often difficult to determine.

**Treatment.**—The treatment of persistent hypotension varies with the cause. In all cases the patient's habits and method of living must be carefully reviewed. If ready physical exhaustion is the dominant feature, rest is important; on the other hand, if the tendency is to mental rather than physical tire, systematic exercise may produce excellent results. In both groups of cases hydrotherapy is invaluable. If myocardial weakness is a factor digitalis is likely to prove efficacious. In the anemic, iron and other tonics are useful. Organotherapy is not often of service, although ovarian or corpus luteum extract may sometimes be given with advantage in hypotension developing at the menopause and epinephrin or an extract of the suprarenal gland may occasionally be of benefit when hypotension is accompanied by features suggestive of Addison's disease. Timme[1] describes a pleuriglandular syndrome characterized by intratemporal headache, great fatigability, low blood pressure, low blood-sugar content, abnormalities of skeletal growth and usually sex deficiencies, in which pituitary gland products cause marked improvement.

[1] Med. Clin. of North America, Jan., 1919.

# DISEASES OF THE MEDIASTINUM

The most important lesions of the mediastinum, exclusive of those affecting the aorta, trachea and esophagus, which are considered under other headings, are mediastinitis, lymphadenitis, lymphomas, morbid growths and emphysema.

## MEDIASTINITIS

Mediastinitis, or inflammation of the connective tissue within the mediastinum, is usually either suppurative or productive.

**Suppurative mediastinitis,** that is mediastinal abscess, may be of traumatic origin, but more frequently it is secondary to septic processes in the tracheo-bronchial lymph-nodes, pleura, lungs, pericardium, esophagus, or vertebræ. Occasionally it develops in the course of acute infections, such as erysipelas, septicemia, scarlatina, etc., although under these circumstances, it is usually the consequence of suppurative lymphadenitis. In rare instances it is caused by the downward extension of an abscess in the neck or a retropharyngeal abscess. Chronic abscess is frequently of a tuberculous nature.

*Symptoms of Mediastinal Abscess.*—Substernal pain and tenderness to pressure over the sternum are the most constant symptoms. In the acute cases fever, chills, sweats, leucocytosis, etc. may be present. Pressure effects, other than moderate dyspnea, are not common, but cough, hoarseness or aphonia, engorgement of the veins of the head and arm, dysphagia, etc. may occur. Physical signs are often meagre. In some cases, however, edema or even a fluctuating swelling is apparent at the episternal notch or the border of the sternum, dulness is evident on heavy percussion, and an irregular shadow is shown by roentgenographic examination.

Absence of thrill, diastolic shock, bruit and expansile pulsation are opposed to aneurysm, but exclusion of the latter is not always easy, for aneurysm sometimes lacks its most characteristic signs and an abscess, owing to the proximity of the great vessels, may, at least, show some pulsation. In doubtful cases a fine aspirating needle may be safely used.

A mediastinal abscess may perforate externally or into the trachea or esophagus, the resulting cavity sometimes refilling and emptying at intervals, and occasionally it burrows down into the abdomen. Not rarely, particularly in cases of chronic abscess, the pus remains circumscribed and ultimately becomes inspissated. *Treatment* is surgical and consists in evacuation and drainage.

**Productive mediastinitis** is characterized by an increase in the fibrous tissues of the mediastinum. It is usually associated with adhesive pericarditis (indurative mediastinopericarditis), the heart and pericardium being bound by adhesions to the chest wall, pleuræ, lungs, and tissues of the mediastinum. In some cases the pleuræ are thickened and partially or totally obliterated, and in others there is also a chronic proliferative peritonitis

with more or less ascites (multiple serositis). This condition is not rarely tuberculous. The symptoms of productive mediastinitis are those of chronic adhesive pericarditis.

## LYMPHADENITIS

Inflammation of the mediastinal lymph-nodes is common. It occurs in all bronchial and pulmonary infections, and in many of the acute specific diseases, such as measles, pertussis, influenza, etc. It is almost constantly present in pulmonary tuberculosis and not rarely tuberculosis of the tracheobronchial nodes exists as a primary condition. Unless there is pronounced swelling of the affected nodes, as in some of the tuberculous cases, the symptoms and physical signs of mediastinal lymphadenitis are usually too indefinite to admit of an exact diagnosis. Large nodes may cause pressure symptoms, such as brassy cough, dyspnea, respiratory stridor, hoarseness, dull pain, etc. Objectively, dulness is sometimes obtained on percussion at the borders of the manubrium or on either side of the upper thoracic vertebræ and the x-ray picture may show definite shadows. Other signs to which more or less importance has been attached are venous murmurs at the root of the neck (Eustace Smith's sign) and prolongation of the whispered voice over the upper thoracic vertebræ (D'Espine's sign). The etiologic factor can be determined only by attention to the history of the patient and a study of his general condition.

Simple adenitis may end in recovery or subside leaving the nodes slightly enlarged and indurated. Suppuration may occur, but it is observed chiefly in the tuberculous form. Perforation into the bronchi, trachea, lungs, pleura, pericardium, esophagus or large vessels occasionally occurs. The contraction of a lymph-node which has become attached to the esophagus may produce in the latter a traction diverticulum.

### LYMPHOMAS

Mediastinal lymphomas may form the chief lesion in leukemia and Hodgkin's disease. In some cases, especially of those involving the thymus, the process closely approaches a malignant tumor (leukosarcomatosis), in that destructive local infiltrations and even distant metastases occur. In all cases brassy cough, hoarseness, respiratory stridor, dyspnea and other pressure effects are much more common than in simple or tuberculous lymphadenitis. In the leukemic form the blood-picture is characteristic, but in mediastinal Hodgkin's granuloma, without enlargement of the palpable lymph-nodes, an exact **diagnosis** is often difficult or impossible.

**Treatment.**—Roentgen irradiation and the administration of arsenic are the only measures likely to be of service, and these cannot produce more than temporary improvement.

### MORBID GROWTHS

True neoplasms of the mediastinum may have their origin in adjacent organs, such as the lungs, pleuræ, or thyroid; they may appear as metastatic growths from distant organs; or they may develop primarily from structures within the mediastinum, usually the thymus or lymph-nodes. More than one-half of mediastinal new growths are primary, and the common site of

origin is the anterior mediastinum. Of 60 cases of primary tumors studied by Ross[1] 44 were sarcoma or lymphosarcoma and 10 carcinoma. Benign tumors are very rare, the most common, perhaps, being the dermoid cyst, of which about 75 cases have been recorded in the literature.

**Symptoms.**—Pressure effects occur in virtually all cases, the most constant being dyspnea, substernal pain, cyanosis, brassy cough, hoarseness or aphonia, inequality of the pupils, dilatation of the veins of the head, arm and upper chest, and dysphagia. A pleural effusion is present in many cases, and often it is hemorrhagic. Hemoptysis is not uncommon. Night-sweats may also occur. Fever occasionally develops as a result of super-added infection. Clubbing of the fingers has been noted. Ultimately, the patient becomes anemic and cachectic.

Percussion may reveal an area of dulness extending in various directions from the mediastinal region and dislocation of the heart. The most common auscultatory sign is weakness or suppression of the breath sounds over the dull area, although exceptionally the breath sounds are harsh or bronchial. The x-ray shows a definite shadow Occasionally there is bulging of the sternum. Cells of the tumor have rarely been found in the sputum, but in a number of instances the expectoration of hair has led to a positive diagnosis of dermoid cyst.

Involvement of the pleuræ, lungs, trachea, pericardium, heart, or great vessels occurs in the large majority of cases. Metastasis to the liver, pancreas, brain, etc., is also common. The *duration* varies from a few weeks to two years. Death may be due to exhaustion, asphyxia, superimposed infection, hemoptysis, or metastases.

**Diagnosis.**—Mediastinal tumor may be confused with pulmonary tuberculosis, thoracic aneurysm, substernal goiter, and the lymphomas of leukemia and Hodgkin's disease. Persistent absence of tubercle bacilli from the sputum, marked dyspnea, the localization of the physical signs and fluoroscopic shadows in the mediastinal region, and such pressure effects as paralysis of the recurrent laryngeal nerves, inequality of the pupils and venous ectasia of the neck and chest will usually serve to exclude *tuberculosis*. The resemblance to *aneurysm* is occasionally very close. Thrill, diastolic shock, diastolic murmur, and bruit are rarely present in tumor. Pulsation, unless it is definitely expansile, and tracheal tug are less important, as they may occur in tumor as well as in aneurysm. Evidences of syphilis and typical anginoid pains are in favor of aneurysm, while rapid deterioration of the general health points to tumor. In *substernal goiter* symptoms of hyperthyroidism are sometimes present and, unless the thyroid is completely intrathoracic and wedged in the mediastinum, which is somewhat exceptional, the neck may be swollen or a tumor may be felt or seen above the sternum during coughing or swallowing. Occasionally, there is a history of the sudden disappearance of a cervical goiter with coincident development of obstructive respiratory symptoms. *Leukemic lymphomas* may be distinguished by the blood-picture and usually by enlarged lymph-nodes in other parts of the body. The lymphomas of Hodgkin's disease, if confined to the mediastinum, may be indistinguishable from mediastinal tumor.

**Treatment.**—This is, as a rule, palliative. Operative measures have been attempted, but, except in cases of dermoid cyst, with little or no success. Roentgen ray or radium should be tried.

[1] Edinburg Med. Jour., Dec., 1914.

## EMPHYSEMA OF THE MEDIASTINUM

The presence of air in the cellular tissue of the mediastinum is usually due to tracheotomy or to injury of the respiratory passages or lungs resulting from penetrating wounds or fractured ribs. Occasionally it is due to perforation of the lung by a tuberculous ulcer or by an abscess, or to bursting of the air-vesicles during a violent paroxysm of cough, such as may occur in pertussis. The condition is frequently associated with interstitial pulmonary emphysema and pneumothorax, but the latter may be absent if rupture of the lung occurs near the root of the viscus or the alveoli burst without injuring the pleura. Important manifestations are the replacement of the cardiac dulness by a tympanitic note and the occurrence of fine râles in the mediastinal region synchronous with the cardiac action (Hoffmann). In many cases cutaneous emphysema supervenes.

# DISEASES OF THE KIDNEYS

## ABNORMALITIES OF THE URINE

### POLYURIA

The quantity of urine is increased whenever more blood flows through the kidneys, either as a result of higher arterial pressure, without constriction of the renal arteries, or of local dilatation of the renal arteries, without change in the general blood pressure. It also is possible that certain substances in the blood may increase the output of urine by directly stimulating the secretory activity of the renal epithelium. Clinically, polyuria, or an excretion of urine in larger amounts than the average daily quantity (1000 to 1500 c.c.), may be transitory or persistent. Transitory polyuria is common. It may be due to the ingestion of large quantities of fluid, the suppression of perspiration, the administration of diuretics, the crisis of a febrile infection, the absorption of a serous effusion, the removal of some temporary obstruction in the urinary passages, trauma of the head, or certain functional nervous disturbances, such as emotional excitement, neuralgic attacks, hysteria, etc.

Persistent polyuria may be due to (1) Diabetes mellitus; (2) diabetes insipidus, or (3) certain chronic diseases of the kidneys, notably chronic glomerulonephritis, renal sclerosis, polycystic kidneys and amyloid kidneys. Occasionally it is observed in pyelonephritis. The most pronounced polyuria occurs in diabetes mellitus and diabetes insipidus, in which diseases the urine occasionally reaches the enormous amount of 30 liters or more.

### OLIGURIA AND ANURIA

**Oliguria,** diminution in the quantity of urine, occurs in acute febrile diseases, in conditions causing profuse sweating or diarrhea, in all conditions which impede the renal circulation, such as decompensated cardiac disease, ascites, pulmonary lesions, etc., and in certain inflammatory or degenerative affections of the kidneys themselves. **Anuria,** or total suppression of urine, may be obstructive or non-obstructive. Obstructive anuria results from compression of both ureters, occlusion of both ureters by calculi, clots, etc., or compression or occlusion of one ureter, if the other kidney is absent or functionless. Non-obstructive anuria may occur in acute nephritis and in the final stages of other organic diseases of the kidneys, occasionally after abdominal operations or injuries, even urethral catheterization (reflex ischemia or paralysis), and rarely in hysteria. Persistent anuria ends in fatal uremia. This symptom complex usually develops in the course of a few days, but exceptionally it does not appear for two weeks or even a longer period. In obstructive anuria the uremia is of asthenic or latent type (see p. 760).

### ALBUMINURIA

The term albuminuria is used to designate the presence of serum-albumin and serum-globulin in the urine.

Albuminuria may be *renal* or *extrarenal* (*accidental*).

Renal albuminuria usually depends on changes in the epithelial cells of the kidney which render them abnormally pervious to the proteins of the blood. Extrarenal or accidental albuminuria is due to the admixture of such albuminous fluids as pus, blood, chyle, etc. with the urine. In this form the amount of albumin is rarely large and is proportionate to that of the foreign protein-containing substance. A disproportionate amount of albumin and the presence of casts in any considerable number point strongly to the coexistence of renal disease.

Clinically, renal albuminuria may occur in the following conditions:

1. *Definite Organic Disease of the Kidneys.*—Albuminuria is one of the important indications of nephritis, although it is observed in many other conditions. Indeed, pronounced albuminuria, especially if it persists and is accompanied by cylindruria, almost always signifies one of the diffuse kidney disorders commonly known as Bright's disease. It must be borne in mind, however, that albuminuria may be absent in nephritis, at least for a time, even when the lesions are serious. The amount of albumin excreted varies from a mere trace in many cases of renal sclerosis and of chronic glomerulonephritis to as much as 3 per cent. or more in acute and subacute tubular nephritis. As a rule, the amount excreted is less than 1 per cent. Other organic diseases of the kidneys, such as amyloid degeneration, abscess, tuberculosis and tumor, by impairing the nutrition of the epithelium, also produce a variable degree of albuminuria. In amyloid kidney, as contrasted with the ordinary forms of nephritis, the serum-globulin in the urine is not rarely in excess of the serum albumin.

2. *Nutritional Disturbances in the Renal Epithelium Induced by Defective Circulation, Severe Infections, Many Forms of Intoxication, General Anemias and Certain Nervous Disorders.*—Both active and passive congestion of the kidneys are accompanied by albuminuria. The amount of protein in the urine is usually small, although occasionally in the passive congestion resulting from myocardial insufficiency it is large. The slight albuminuria occurring in acute infections, such as typhoid fever, diphtheria, erysipelas, measles, etc., is apparently due to cloudy swelling of the renal epithelium, a condition more closely related to the toxins causing the fever than to the elevation of temperature itself. The albumin usually appears late, when the structural changes are most pronounced, and disappears during convalescence. A great variety of irritants, other than the toxins produced by pathogenic organisms, are capable of damaging the renal epithelium sufficiently to permit the transudation of albumin. Thus, mercurials, salicylates, copaiba, etc. in large doses, etherization and chloroformization, jaundice, (bile pigments), and diabetes (sugar) frequently cause slight albuminuria. The albuminuria of pregnancy is doubtless also of toxic origin, although pressure on the renal veins by the enlarged uterus may sometimes be a contributing factor. Inasmuch as the urine in toxic conditions may contain a few tube-casts in addition to albumin, it is obvious that no sharp line can be drawn between toxic albuminuria and the milder forms of nephritis.

Whether the albuminuria occurring in general anemia is due in part to changes in the blood which renders its albumin more diffusible or is wholly the result of nutritional disturbances in the renal cells is not clear. The immediate cause of the albuminuria occurring in epilepsy, cerebral hemorrhage, tetanus and other diseases of the nervous system is probably variable, but changes in the renal circulation are usually assumed to be an important factor.

3. *Intermittently in certain healthy individuals*, it is a well established fact that albumin may be excreted at intervals in the urine in the absence of

any recognizable diseases or intoxication. This form of albuminuria is seen chiefly between the ages of 10 and 25 years.

Moxon[1] termed it *albuminuria of adolescence or remittent albuminuria* and Pavy[2] renamed it *cyclic albuminuria*. Subsequently it was called *physiologic* or *functional albuminuria*. Because albuminuria is remittent or cyclic, it does not follow that it belongs to this class. In chronic nephritis the albuminuria is often much less pronounced in the morning than in the evening, and if slight it may even disappear entirely after a night's rest. Not infrequently in the functional cases the albumin appears only after cold bathing, mental excitement, or physical exertion. It has been shown that after strenuous muscular exercise, such as is required in Marathon races, not only albumin, but also a few tube-casts and a small percentage of erythrocytes regularly appear in the urine. In other cases of so-called physiologic albuminuria the chief factor is the assumption of an erect posture, a maximum amount of albumin being found in the forenoon, a minimum amount in the evening, and none at all during the night or immediately after rising. Even in the forenoon the amount is usually small, although it occasionally may exceed $\frac{1}{10}$ of 1 per cent. Tube-casts are rarely present. For this particular form of albuminuria Stirling[3] proposed the term "*orthostatic*" albuminuria and Heubner[4] that of "*orthotic*" albuminuria. Occasionally, the condition is hereditary and familial. Most of the subjects are poorly nourished, show evidences of vasomotor instability and have a low blood pressure. The exact nature of the disturbance is still unknown. Lenoir, Kuttner, Sutherland[5] and others lay stress upon abnormal mobility of the kidneys. Lüdke and Sturm, von Jagic, Reyher[6] and others believe that it is often an early expression of pulmonary tuberculosis. Jehle[7] has emphasized the importance of lumbar lordosis as an etiologic factor, and Erlanger and Hooker[8] that of diminished pulse pressure.

Even in the absence of cylindruria, polyuria, cardiovascular changes, and impairment of the functional efficiency of the kidneys, as shown by chemical tests, it is unwise to class an albuminuria as orthostatic until the patient has been under observation for many months, since in a certain proportion of such cases signs of organic disease ultimately reveal themselves. The older the patient, the more pronounced the albuminuria, and the longer it persists the greater the probability of nephritis.

## ALBUMOSURIA AND BENCE-JONES PROTEINURIA

Albumosuria is a term used to denote the presence in the urine of proteoses, the latter being intermediate products of the digestion of proteins and frequently, but incorrectly, referred to as albumoses. Proteoses are not coagulated by heat, but may be detected by acidifying the urine with acetic acid, boiling, filtering while hot, and treating the filtrate with trichloracetic acid, which yields a white precipitate.

Albumosuria may occur whenever a large amount of tissue or cellular exudate is undergoing autolysis and absorption. It has been observed in suppurating processes of all kinds, including advanced pulmonary tubercu-

[1] Guy's Hosp. Reports, 1878.
[2] Lancet, 1885.
[3] Lancet, 1887.
[4] Ueber Chron. Nephritis u. Albumin. in. Kind., Berlin, 1897.
[5] Amer. Jour. Med. Sci., Aug., 1903.
[6] Monat. f Kinderheilk., 1913, xii, No. 3.
[7] Münch. med. Woch., 1908, lv, 12.
[8] Johns Hopkins Hosp. Rep., 1904, xii, 145.

losis, in pneumonia during the stage of resolution, in malignant growths, in involution of the puerperal uterus, in leukemia, in acute yellow atrophy, etc.

**Bence-Jones Proteinuria.**—The protein first described by Bence-Jones[1] in 1847 was formerly considered an albumose, but it is now known to be a peculiar protein, probably originating in an interrupted or abnormal synthesis of some normal body protein (Taylor, Miller and Sweet[2]). It is peculiar in readily passing through kidneys which hold back the normal serum proteins. Strong hydrochloric acid precipitates it, but not acetic acid, and with strong nitric acid it forms a precipitate, which disappears on heating and reappears on cooling.

Bence-Jones protein has been found in the urine, periodically or continuously, in small or large amounts (6 per cent. or more), most frequently in multiple myeloma, a specific malignant tumor of the bone-marrow, but it is not pathognomonic of this condition, nor is it always present in myelomatosis. It has been found occasionally in leukemia, in carcinomatous bone metastasis, and perhaps in osteomalacia, and more recently Miller and Baetjer[3] have described it as the only protein excreted in the urine in certain cases of chronic nephritis with high blood pressure.

## GLYCOSURIA

### (Glucosuria; Glycuresis)

The term glycosuria is used to designate the excretion of glucose (dextrose) in the urine in larger quantities than the mere traces normally present. Clinically, it occurs under the following conditions·

1. In diabetes mellitus. In this disease the sugar is excreted persistently and in considerable quantity—from 0.5 to 10 per cent.

2. In health, if the ingestion of glucose is excessive (alimentary glycosuria).

3. In various lesions and functional disturbances of the nervous system, such as punctute of the floor of the fourth ventricle (piqûre of Bernard), concussion of the brain, cerebral hemorrhage, cerebral tumor, extreme excitement, etc.

4. In certain affections of the ductless glands other than the pancreas, especially in hyperthyroidism and acromegaly.

5. In poisoning by phloridzin, chloroform, chloral hydrate, alcohol, amyl nitrite, phosphorus, carbon monoxid, epinephrin, thyroid extract, mushrooms (Amanita muscaria), and many other substances.

6. Sometimes in metabolic disorders in which ductless glands may not be concerned, as gout and obesity.

7. Occasionally in acute infectious diseases.

8. In so-called renal diabetes.

9. Sometimes in pregnancy.

Except in poisoning by phloridzin and certain other substances and in so-called renal diabetes, glycosuria always depends upon an excess of sugar in the blood, that is, upon hyperglycemia. The glucose concentration of normal blood ranges from 0.06 to 0.14 per cent. Ordinarily, when the concentration exceeds 0.17 or 0.18 per cent. some of the sugar escapes in the urine. In certain diseases, however, notably nephritis and many cases of severe diabetes of long duration, the renal threshold becomes much higher. Indeed, in some of the most severe cases of diabetes the urine at times

[1] Philos. Trans. Royal Soc., 1848, Pt. I.
[2] Jour. Biolog. Chem., 1917, 29, 425.
[3] Jour. Amer. Med. Assoc., Jan. 19, 1918.

contains little or no sugar, even though the glucose concentration of the blood is very high.

The studies of von Mering and Minkowski,[1] Opie and others have made it clear that deficient functionation of the pancreas is the chief, if not the only, cause of *diabetes mellitus*. Apparently, the pancreas is the only organ the loss of which is followed by this disease. The exact relationship of the pancreas to carbohydrate metabolism is still obscure, although it is certain that the gland forms an internal secretion, which is in some way essential to the utilization of sugar. This internal secretion is believed to have its source in the islands of Langerhans. The sugar excreted by diabetics is derived from carbohydrates of the diet and sometimes from proteins, either of the diet or the tissues.

Normal individuals are able to take from 150 to 500 grams of glucose on an empty stomach without excreting sugar in the urine (Taylor and Hulton[2]), the limit depending not only upon the capacity to utilize carbohydrate, but also upon the degree of permeability of the kidneys for sugar. Glucose in amounts larger than those stated are usually productive of glycosuria (*alimentary glycosuria*). The occurrence of the latter is favored by alcoholic drinks, certain poisons and infections, and is hindered by physical exertion. Glycosuria following overindulgence in starchy food (glycosuria ex amylo) is probably always abnormal and points strongly to diabetes mellitus. Cane sugar in excess is eliminated in small part unchanged, but rarely in healthy persons as glucose. Normally, the ingestion of large amounts of fructose (levulose) is followed by the appearance of glucose in the urine, sometimes with traces of unchanged fructose. The appearance in the urine of fructose in considerable quantity (alimentary fructosuria) is often observed in diabetes and in degenerative diseases of the liver. Alimentary glycosuria is not accompanied by any serious disturbance, but it sometimes merges into diabetes mellitus, and if it occurs readily it should always arouse suspicion of pancreatic insufficiency.

The glycosuria resulting from *Bernard's puncture of the medulla* is caused by excessive unloading or "mobilizing" of the hepatic glycogen in the form of glucose, an effect which is due, however, not to any direct stimulation of the liver, but to an influence exerted on that organ through the sympathetic system and the adrenals, for no sugar appears in the urine after ablation of the adrenals or division of the splanchnic nerves. It is likely that the glycosuria resulting from *psychic shock* and *nervous disturbances* generally is also due to stimulation of the glycolytic center in the medulla and over activity of the adrenals. Apparently the internal secretions of the adrenals and pancreas are mutually antagonistic (Falta, Eppinger Rudinger,[3] and Zuelzer[4]), and either excessive activity of the adrenals or insufficient activity of the pancreas may exaggerate glycolysis in the liver and thus cause glycosuria. The functions of the ductless glands are closely correlated and it is probable that the glycosurias of *hyperthyroidism* and of *acromegaly* are due to overactivity of the adrenals or to a more direct depression of the endosecretory activity of the pancreas.

*Toxic glycosuria* is probably brought about in different ways by different poisons. Epinephrin stimulates glycolysis directly or indirectly by depressing the pancreas. Morphin, chloral hydrate, amyl nitrite and many other drugs in large doses apparently act on the glycolytic centre. Others, like

[1] Centralbl. f. klin. Med., 1889, 394.
[2] Jour. Biol. Chem., 1916, xxv, 173.
[3] Ztschr. f. klin. Med., 1908, lxvi, 1.
[4] Deutsch. med. Woch., 1908, xxxiv, 1380.

phloridzin, acting solely by lowering the renal threshold for sugar. Prolonged chloroformization produces glycosuria, at least in part, by reducing the glycogenetic function of the liver. The mechanism of the transitory glycosurias occurring in *gout*, *obesity*, and the *acute infections* is not clear, although doubtless it varies even in the same disease.

The term *renal diabetes* is used to designate a comparatively rare anomaly characterized by a persistent glycosuria, which is but little influenced by diet, which is not dependent upon any abnormally high level of blood sugar, and which is not associated with any of the classical symptoms of diabetes mellitus. The condition, which was first described by Klemperer[1] in 1896, is assumed to be due to a specific renal defect consisting merely in a lowering of the normal threshold for sugar excretion. It is relatively harmless, but is not influenced materially by dietetic or medicinal measures. Lewis and Mosenthal[2] have given an excellent review of the cases reported up to 1916.

While lactosuria is common in *pregnancy*, true glycosuria is relatively rare, although it sometimes develops in the last weeks of gestation. The cause of it is not known. In some cases, at least, it seems to be of the alimentary type. The sugar usually disappears from the urine at the conclusion of labor, but occasionally actual diabetes supervenes.

## FRUCTOSURIA

### (Levulosuria)

Fructose, or fruit sugar, is not rarely excreted along with dextrose in diabetes mellitus (mixed mellituria). Alimentary fructosuria may be observed in healthy persons after the ingestion of large amounts of fructose (100–200 grams); it often occurs in chronic diseases of the liver, especially cirrhosis, after the ingestion of comparatively small amounts of fructose (50 to 100 grams); and it is occasionally noted in healthy persons after the ingestion of fructose in quantities no larger than ordinarily occur in the food. In alimentary fructosuria the excretion of fructose always ceases when the diet is carbohydrate free. Finally, there is a rare anomaly of metabolism, analogous to that causing pentosuria, in which fructosuria is persistently present and is uninfluenced by the diet (essential fructosuria).

## PENTOSURIA

Pentosuria, or the excretion in the urine of sugars containing five atoms of carbon, is uncommon. It sometimes accompanies glycosuria in diabetes mellitus and occasionally it is observed after the ingestion of large quantities of foods rich in pentose, such as cherries, plums, apples, etc. (alimentary pentosuria). In rare instances it occurs as an independent anomaly of metabolism and to this form, which may or may not be familial, the term *essential pentosuria* has been applied. About 40 cases are on record, the condition is intractable, but it occasions no systemic disturbance and is clinically important only because of its liability to be mistaken for diabetes mellitus. The pentoses react slowly but strongly with Fehling's solution, but do not ferment with yeast. The source of the sugar in essential pentosuria remains obscure. It may be in galactose formed from glucose or in nucleo-proteins. It is not alimentary, for the condition persists despite a carbohydrate-free diet. Although the total pentose content of the body does not exceed 20 grams, outputs of pentose as high as 36 grams have been reported.

[1] Verein f. inn. Med., May, 1896.

[2] Johns Hopkins Hosp. Bull., 1916, xxvii.

## KETONURIA

The term ketonuria is employed to designate the presence in the urine of ketones (acetone bodies)—acetone, diacetic acid, and beta-oxybutyric acid. The ketones are products of the incomplete oxidation of the fatty acids formed from fats and also, under certain conditions, from amino-acids derived from proteins. It is generally assumed that beta-oxybutyric acid is the mother substance and is decomposed first to diacetic acid and then to acetone. Under normal conditions the ketones are ultimately oxidized to carbon dioxid and water, so that the urine contains, at most, but traces of acetone. However, under certain abnormal conditions, especially when there is a serious disturbance carbohydrate metabolism, as in diabetes mellitus, when there is a pronounced deficiency of carbohydrates, as in starvation, or when there is excessive breaking-down of proteins, as in inanition and cachexia, these bodies may escape oxidation and appear in the urine unchanged. In no condition is ketonuria so marked as in severe diabetes mellitus, with a disability of the body to utilize the carbohydrates.

"Fats burn only in the fires of the carbohydrates" (Rosenfeld) and when the latter are deficient the body "smokes" with unburnt fats—ketones (Woodyatt[1]). Ketonuria is also observed in starvation, however produced, in chloroform narcosis, in the toxemias of pregnancy, in the recurrent (cyclic) vomiting of early childhood, and less constantly in acute infections, diarrheal diseases, carcinoma, and poisoning by various drugs.

Acetone may appear in the urine without diacetic acid, and both of these substances may appear without beta-oxybutyric acid, but the latter is never present without diacetic acid and acetone. Pronounced ketonuria is usually a precursor or an accompaniment of systemic intoxication, which may culminate in coma (see p. 368), but not invariably, for in some cases the excretion of the acids is so rapid that no reduction of the $CO_2$-carrying capacity of the blood, or acidosis (see p. 386), ensues. On the other hand, as acidosis may be due to a retention of acid phosphates in the blood or an excessive accumulation of carbon dioxid, it is evident that it may occur independently of ketonuria. In diabetic coma the daily excretion of oxybutyric acid in the urine may amount to 50 grams or more and that of diacetic acid and acetone together to 8 or even 10 grams.

## CYLINDRURIA

Tube-casts are cylinders of albuminous material formed in the uriniferous tubules. At the present time two theories are held as to their origin; according to the one, they are produced by the coagulation of albuminous bodies that have escaped from the blood into the uriniferous tubules, and according to the other they are composed of substances derived from the renal epithelium. Many casts contain in addition to a homogeneous hyaline matrix epithelial cells, blood corpuscles, pus cells, or the products of degenerated epithelium, such as granular detritus and fat-droplets. The following varieties are recognized: Hyaline, waxy, epithelial, granular, blood, and pus.

*Hyaline casts* are clear transparent cylinders, often so pale as to be scarcely visible. They are usually straight or slightly curved, but they may be convoluted. *Waxy casts* resemble hyaline casts, but they are less transparent and more rigid, and are often slightly yellow. They are probably hyaline casts that have been retained for some time in the uriniferous tubules.

*Epithelial casts* are hyaline casts covered more or less closely with epithelial cells from the tubules. *Granular casts* are hyaline casts which are

[1] Jour. Amer. Med. Assoc., June 17, 1916.

imbedded with the débris of disintegrated epithelial cells. The granules may be fine or coarse and pale or dark. *Fatty casts* are hyaline cylinders more or less thickly studded with fat globules. They are also products of epithelial degeneration, and frequently a single cast will show epithelial cells, granular matter, and fat-droplets in varying proportions. *Blood casts* are cylindric masses of blood-cells, chiefly erythrocytes, or more commonly hyaline casts with blood-cells adherent. *Pus casts* are hyaline casts to which pus cells are attached.

*Cylindroids* are formations resembling hyaline casts, but they differ from the latter in having a more irregular outline and in being broad at one end and tapering to a long slender tail. They probably consist of mucus.

**Significance of Tube-casts.**—A few hyaline casts are frequently found in the urine of healthy persons. Their presence, however, probably always signifies slight irritation or congestion of the kidneys, although such changes may be only transitory. Even an occasional granular cast in the urine of persons past middle life, who present neither albuminuria nor cardiovascular changes, may have little significance. Nevertheless, hyaline casts or granular casts in large numbers, and other casts in any number, point strongly to organic disease of the kidneys, usually nephritis. In this condition the urine also contains albumin, although the amount of the latter and the number of casts are not necessarily proportional. Renal albuminuria may occur without casts and occasionally casts are present without albumin. Almost any variety of cast may be found in any form of nephritis. However, epithelial casts and fatty casts, especially if present in large numbers, point to marked desquamation and degeneration of the renal epithelium, such as occurs in tubular nephritis; blood-casts denote hemorrhage into the tubules, which is most common in acute nephritis or acute exacerbations of chronic nephritis, particularly of the glomerular type; and casts containing numerous pus cells are rarely observed except in suppurative pyelonephritis. Waxy casts in rare instances give an amyloid reaction, but this does indicate any amyloid change in the kidney itself; indeed, waxy casts do not necessarily mean that the renal changes are chronic, as was formerly supposed. Cylindroids have little significance unless they occur in large numbers, when they indicate renal irritation.

As tube-casts rapidly disintegrate in the presence of bacteria, it is necessary in searching for them to use freshly voided urine, or a sample that has been preserved by being kept on ice or by the addition of formalin (1 drop to 4 ounces) or a few grains of thymol.

## HEMATURIA

The most common causes of hematuria are: (1) Tumor of the kidney, bladder or prostate; (2) tuberculosis of the kidney or bladder; (3) stone in the kidney, ureter or bladder; (4) acute or chronic nephritis; (5) active or passive congestion of the kidneys, (6) acute cystitis; (7) various general diseases affecting the blood, such as scurvy, purpura, leukemia and grave infections; (8) traumatism affecting any part of the urinary tract.

Less frequently hematuria is caused by one of the following diseases of the kidney: Infarct, abnormal mobility, polycystic degeneration, hydronephrosis, and aneurysm of the renal artery. In some instances it is due to enlarged prostate with vesical varicosities. In certain tropical regions vesical bilharziasis and filarial disease (hematochyluria) are relatively common causes. Hematuria has not rarely been observed in the course of appendicitis (ureteritis or concomitant congestion or inflammation of the right kidney). Occasion-

ally it is induced by gonorrhea. The passage of uric acid or calcium oxalate crystals in large quantities may cause slight bleeding. The administration of hexamethylenamin in large doses, especially if the urine is highly acid, may be followed by both painful micturition and hematuria (renal or more frequently vesical irritation). Rarely hematuria results from pregnancy (renal congestion or pyelitis). Occasionally hematuria may be traced to vascular tumors of the urethra or to urethral varices. It has been observed in Raynaud's disease, although much less frequently than hemoglobinuria. Finally, hemorrhage from the kidney sometimes occurs in the absence of any recognizable cause, and under such circumstances it has been variously described as essential or idiopathic hematuria, renal epistaxis, angioneurotic hematuria, etc. In not a few of the cases, however, definite lesions have been discovered at operation; thus, there has been found circumscribed or diffuse nephritis, undue mobility of the kidney, disseminated or localized telangiectasis, pyelitis with congestion of the renal papillæ, or calcareous incrustation of the papillæ.

**Diagnosis.**—The blood may be detected by the naked eye or only by microscopic examination. When from the kidney it is usually more intimately mixed with the urine than when from the bladder. Renal blood, however, sometimes forms clots and the shape of these may betray their origin. Fragmentation and decolorization of the red cells is suggestive of renal hematuria, unless the blood has remained a long time in the bladder or the reaction of the urine is strongly alkaline or acid. When the bladder is the source of hemorrhage the first portion of urine voided may be clear and the last portion bloody, and when the hemorrhage is from the urethra the first portion of urine voided is usually bloody and the last clear. However, too much importance should not be attached to these points. In many cases the source and cause of the bleeding can be determined only by careful consideration of the clinical history and the data obtained from cystoscopy, ureteral catheterization, and roentgenographic studies, including, if necessary, pyelography, and chemical tests for renal efficiency. Before regarding a case of profuse painless hematuria as one of "essential hematuria" every effort should be made to exclude tumor, tuberculosis and nephritis. Hemorrhage from the kidney is not rarely the initial symptom of nephritis, especially of streptococcus nephritis in children. Slight bleeding may also be the first indication of infantile scurvy. In women the finding of a few erythrocytes in the urine is without significance, unless the specimen has been obtained by catheterization.

**Treatment.**—This varies with the cause of the hematuria. If the hemorrhage is profuse, the immediate indications are to keep the patient at rest in bed, to restrict the diet to bland foods, and to reduce the concentration of the urine by allowing liberal amounts of drinking water. Epinephrin, pituitary extract, tannin, etc. are useless when administered internally. If the patient is restless and excited morphin may be given with advantage. Epinephrin solution (1:2000) may be of service in vesical hemorrhage if injected into the bladder, and also, according to Braasch, in some cases of so-called essential hematuria, if injected directly into the pelvis of the kidney. In the latter condition, if conservative measures fail and the patient's life is jeopardized by increasing anemia, recourse should be had to surgical treatment (nephrotomy, decapsulation, nephropexy, nephrectomy). Sometimes nephrotomy alone is successful, although the manner of its action is not apparent.

## HEMOGLOBINURIA

By hemoglobinuria is meant the excretion of blood pigment in the urine. According to the intensity of the pigmentation the urine may present a smoky appearance or a dark brownish-red color. Occasionally, it is almost black. Microscopic examination of the sediment reveals opaque red granules, but very few, if any, red blood cells. With the spectroscope the characteristic bands of hemoglobin or, more frequently, of methemoglobin are seen. Finally, when the urine is layered under a mixture of equal parts of a fresh 1 per cent. alcoholic solution of guaiacum and oil of turpentine, as in Heller's test for albumin, there is formed at the line of contact a blue ring, which is not dissipated by heat.

Care must be taken, of course, to distinguish between a true hemoglobinuria and a hematuria in which the corpuscles, although originally present, have been dissolved owing to decomposition of the urine.

According to Pearce and his associates,[1] free hemoglobin is not removed by the kidneys until its concentration in the blood serum reaches 0.06 gram per kilo of body weight, and that when the concentration exceeds 0.2 gram per kilo of body weight choluria also occurs. These observers also point out that when the erythrocytes are destroyed very slowly the concentration of hemoglobin in the blood may not reach the threshold value of the kidneys and yet it may be sufficient to increase the bile formation to the point of overtaxing the liver and thus cause jaundice.

1. Hemoglobinuria occurs in various forms of poisoning attended by excessive hemolysis. Thus, it may result from the toxic action of potassium chlorate, phenol, arseniuretted hydrogen, iodoform, venom of certain snakes, etc. It is sometimes observed after extensive superficial burns. The injection of the blood or blood serum of certain animals into the veins of other animals induces it, and even the injection of the blood of one human being into the veins of another may result in pronounced hemolysis and hemoglobinuria if the blood of the donor is incompatible with that of the recipient. Occasionally, it appears during the absorption of large hemorrhagic effusions, and under such circumstances it is to be attributed, according to Michaelis,[2] to the liberation of some substance having a strong hemolytic action rather than to the reentrance into the circulating blood of large quantities of hemoglobin.

2. Hemoglobinuria may also be produced by certain infectious diseases, notably malaria, septicemia, and infective jaundice. In regard to African blackwater fever, it is generally believed that the disease is due to the malarial parasite rather than to quinin, but that at times the administration of the latter favors the occurrence of the hemoglobinuria.

3. Hemoglobinuria is occasionally observed as a periodic or intermittent phenomenon in the absence of any of the causes just mentioned, and then it is known simply as *paroxysmal hemoglobinuria*. This condition may occur at any age, but it is most common in young adults. Males are more disposed to it than females. Syphilis appears to be an important etiologic factor in many instances. Paroxysmal hemoglobinuria is not very rare in the subjects of Raynaud's disease. This association was noted in 11 of 180 cases of Raynaud'[3] disease analyzed by Monro.[3] The attacks are usually brought on by exposure to cold, although occasionally muscular exertion or emotional excitement may be the determining factor. They are frequently accompanied by chill, fever and lumbar pains. In some cases jaundice develops

[1] Jour. of Exper. Med., 1912, xvi, No. 3.
[2] Deutsch. med. Woch., Jan. 24, 1901.
[3] Raynaud's Disease, Glasgow, 1899.

during or after the hemoglobinuric attack, and in others vomiting and diarrhea are conspicuous features. Occasionally urticaria or localized edema also occurs. The disease lasts, as a rule, many years, and only rarely proves fatal. The pathogenesis of this form of hemoglobinuria is somewhat obscure, but the most plausible theory is that the essential factor is the presence in the blood of an autohemolysin which reacts with the corpuscles only under some special condition, usually exposure to cold. The fragility of the corpuscles is apparently not increased.

**Treatment.**—This should be directed to the primary cause. In malarial cases quinin may be used tentatively, but if its effects are unfavorable, it should be withdrawn and methylene blue (3–5 grains—0.2–0.3 gm., three or four times a day) substituted. Paroxysmal hemoglobinuria, if due to syphilis, may yield to mercury and arsphenamin. Widal[1] has obtained good results from repeated subcutaneous injections of the patient's own blood-serum. Cold and fatigue, as far as possible, should be avoided. During the attacks the patient should be kept warm and should be given an abundance of hot liquid. Occasionally nitrites seem to have afforded relief.

## HEMATOPORPHYRINURIA

Hematoporphyrin is an intermediary substance in the transformation of hemoglobin into bilirubin. It is found normally in the urine in traces (Garrod). Pathologic hematoporphyrinuria, with Burgundy-red or reddish-brown urine, has been observed most frequently after the repeated administration of sulphonal or trional, but it has occasionally occurred also in poisoning from veronal, lead, quinin and other drugs; in certain infections, such as typhoid fever, measles, rheumatism, and tuberculosis; in certain gastrointestinal disturbances; in internal hemorrhages; in exophthalmic goiter; and certain skin diseases. Barker and Estes[2] have reported a family form of hematoporphyrinuria in association with gastroduodenal dilatation, peculiar tonic spasms of the muscles and polyneuritis. Hematoporphyrin and other porphyrins apparently act as photosensitizing agents rendering the body peculiarly susceptible to noxious effects of sunlight. In some instances hydroa aestivale—a recurrent vesicular eruption occurring for the most part on the exposed parts, and chiefly in children during the summer months—and certain necrotic conditions of the skin have been observed in association with hematoporphyrinuria (McCall Anderson, Perutz,[3] Hausmann[4]).

## PYURIA

The presence of pus in the urine indicates suppuration in some part of the genitourinary tract or the rupture of an abscess into the genitourinary tract. Thus, it may be associated with the following conditions: (1) such renal lesions as abscess of the kidney, pyonephrosis, pyelonephritis; (2) all forms of cystitis; (3) urethritis, especially of gonorrheal origin; (4) vaginal or uterine catarrh (leucorrhea); (5) prostatitis or prostatic abscess; (6) perinephric, periappendicular or periuterine abscess discharging into the urinary passages.

Urine containing pus is more or less turbid, and on standing throws down a white sediment resembling that of amorphous phosphates, but the nature of which is at once revealed by microscopic examination. The source of the

[1] Semaine Medicale, 1913, xxxiii, No. 52.
[2] Jour. Amer. Med. Assoc., Aug. 31, 1912.
[3] Wien. klin. Woch., 1910, 23.
[4] Biochem. Zeit., 1914, 67.

pus is indicated in various ways. In *renal pyuria* there may be marked constitutional symptoms; local signs—pain, tenderness or tumor—are sometimes present; and the urine often contains tube-casts and a larger amount of albumin than can be accounted for by the admixture of pus. In *vesical pyuria* increased frequency of urination and dysuria are more common than in renal suppuration and there is often pain with tenderness in the region of the bladder. The structure of the epithelial cells accompanying the pus corpuscles is of little significance in the diagnosis between pelvic and vesical catarrh; nor is the reaction of the urine of much assistance, although it is more likely to be alkaline with cystitis than with pyelonephritis. In doubtful cases valuable aid may be afforded by cystoscopic examination. ureteral catheterization, and roentgenographic studies.

In *urethral* and *prostatic suppuration* there are usually definite local signs. The pus may be present only in the urine that is first discharged, the amount is small, and characteristic thread-like formations of pus-cells and mucus are frequently observed. The recognition of *leucorrheal pyuria* is rarely difficult. In doubtful cases urine should be obtained by catheterization. The *rupture of an abscess into the urinary tract* is usually marked by a sudden discharge of pus, profuse, but transient or intermittent. A pyuria of the same character, however, is also observed at times in pyonephrosis.

## LIPURIA, CHYLURIA, CHOLESTEROLURIA

Normally, from 1 to 3 mg. of fat are excreted in the urine daily, the amount varying with the proportion of fat in the diet. In certain pathologic conditions there is a marked increase in the fat of the urine, the latter sometimes being turbid when passed. Microscopic examination usually, but not invariably, reveals refractive globules, which stain black with osmic acid or red with Sudan III. Care must be taken not to mistake for true lipuria accidental contaminations of the urine with fatty materials, such as lubricants. In *pathologic lipuria* the fat may be derived from the blood or from the epithelium of the urinary passages. Thus, it may be observed in diabetes mellitus, phosphorus poisoning, fat embolism, and other conditions associated with lipemia, and also in chronic nephritis, pyelonephritis, and cystitis when fatty epithelium is present. Possibly in some cases of nephritis an abnormal amount of fat may also escape from the blood into the urine, owing to an altered permeability of the renal capillaries or epithelium (Sakaguchi,[1] Sanes and Kahn[2]).

In *chyluria* the urine contains such an enormous number of minute fat droplets or fat-granules that it presents a milky appearance. Albumin, fibrin, and a variable number of blood cells always accompany the fat. Occasionally, the urine coagulates spontaneously on standing and not rarely blood is present in sufficient quantity to impart to the urine a pink hue (*hematochyluria*). The most frequent cause of chyluria is the presence of adult filariæ in the thoracic duct, with stasis of the chyle and the rupture of varicose lymphatics in the urinary passages. In some instances microfilariæ can be found in the milky urine. Occasionally chyluria results from obstruction of the thoracic duct by a thrombus, metastatic tumor, tubercle, or external pressure. The amount of fat in chylous urine is influenced by the diet and often by posture.

Crystals of cholesterol are occasionally found in the urine (*cholesteroluria*) in chyluria and in diseases associated with extensive fatty degeneration of the renal epithelium, such as chronic tubular nephritis and pyelonephritis.

[1] Ztsch. f. klin. Med., 1913, 48, 1.
[2] Arch. Int. Med., Feb., 1916.

## FIBRINURIA

Spontaneous coagulation of the urine, due to the presence of fibrinogen and the formation of fibrin is rare in the absence of blood or chyle. It is occasionally observed, however, in nephritis and in tumor of the kidney with destruction of the renal tissue. O'Conor[1] has collected 25 cases.

## LEUCINURIA AND TYROSINURIA

Leucin and tyrosin are intermediary products of protein cleavage. Their presence in the urine in appreciable quantities is always pathologic, and while it may be observed in any condition in which there is extensive destruction of tissue, it is most frequently associated with disease of the liver of a necrotic type, such as acute yellow atrophy, chloroform necrosis, phosphorus poisoning, puerperal eclampsia, etc.

In acute yellow atrophy of the liver, leucin and tyrosin are sometimes excreted in such large amounts that they are precipitated spontaneously. In most cases, however, the urine must be concentrated by evaporation in order to demonstrate them. Leucin crystallizes in the form of greenish-yellow spheres, often with concentric or radial striations, and tyrosin in the form of very fine needles, usually arranged in sheaves or rosets. It is noteworthy that crystals of ammonium urate and of calcium phosphate may assume similar forms.

## CREATINURIA

Normally, creatin is not present in the urine of adult males, but it occurs regularly in the urine of children, and at times in the urine of women. Creatinuria seems to be in some way related to protein metabolism. It is repressed by a low protein (creatin-free) diet (Denis and Minot[2]) and also by agents that reduce protein catabolism, such as carbohydrates (Steenbock and Gross[3]). According to Rose[4] the adult man can destroy considerable amounts of creatin, the child much less, while the woman, in this respect, occupies a position intermediate between the man and the child. Pathologically creatinuria occurs especially in conditions in which there is increased protein catabolism, such as fevers, hyperthyroidism and certain other endocrine disorders, tumor cachexia, postpartum involution of the uterus, diabetes mellitis, phosphorus poisoning, etc. Janney, Goodhart, and Isaacson[5] observed it also in 9 cases of muscular dystrophy.

## INDICANURIA

Indican (potassium indoxyl sulphate) is formed in the liver from indoxyl, which in turn is produced in the intestine by the bacterial putrefaction of tryptophan, an amino-acid contained in nearly all proteins. Indoxyl is also formed from tryptophan in putrefying tissues and exudates. Whether or not it is formed from tryptophan in intracellular metabolism is not definitely known. The amount of indican excreted in health usually ranges between 5 and 20 milligrams a day, the variations depending upon the freedom of resorption, the character of the intestinal flora, and the type of proteins in

[1] Amer. Jour. of Med. Sci., May, 1920.
[2] Jour. Biol. Chem., 1917, 31.
[3] Jour. of Biol. Chem., 1918, 36.
[4] Jour. of Biol. Chem., 1917, 32.
[5] Archives Int. Med., Feb., 1918.

the diet. With a diet consisting chiefly of fats, carbohydrates and egg-albumin very little indican appears in the urine.

Pathologically, a marked increase in the output of indican is observed in all conditions which favor putrefaction in the bowel, especially occlusion of the small intestine, acute and chronic peritonitis, obstructive jaundice, and many diseases accompanied by diarrhea. On the other hand, diseases of the stomach *per se*, simple constipation and obstruction of the large intestine do not materially increase the excretion of indican. Putrid pus and putrid tissues being other sources of indican, such conditions as chronic empyema, gangrene of the lung, bronchiectasis, putrid carcinoma, etc. favor the occurrence of indicanuria. Indican itself is only slightly toxic, but it is often accompanied by other products of protein putrefaction, such as skatol, cresol, etc., which may cause headache, irritability, insomnia, ready fatigue and other neurasthenic symptoms. The detection of indican in the urine depends upon its decomposition into sulphuric acid and indoxyl and the oxidation of the latter into indigo-blue. Rarely the transformation occurs spontaneously in decomposing urine, with the production of a bluish color. Renal calculi containing indigo have been described by Ord and others.

## UROBILINURIA

Urobilin is derived chiefly, if not solely, from the reduction of bilirubin by bacteria in the intestine. From the intestine the major portion is brought by the portal system to the liver, where, if the organ is normal, it is retained and probably resynthesized to hemoglobin. Possibly at times it may be formed outside of the intestine, in the liver itself, as Wilbur and Addis[1] believe, or in the tissues from disintegrated blood, in hemorrhagic effusions. In hepatic disease urobilin may escape transformation into hemoglobin and be absorbed into the blood, and excreted unchanged in the urine. This may also occur in conditions associated with rapid blood destruction, owing to the great increase in the amount of bilirubin in the feces and the resultant production of urobilin in quantities too large to be absorbed and retained by the liver. As would be expected, the amount of urobilin in the urine is usually considerably increased in certain forms of hepatic disease, such as cirrhosis, passive congestion, cloudy swelling, etc., and also in certain conditions associated with excessive hemolysis, such as hemolytic icterus and pernicious anemia. However, in obstruction of the common bile-duct in severe nephritis, and in profuse diarrhea with rapid removal of the intestinal contents, urobilin may fail to be excreted, even when other conditions favor its appearance in the urine. The degree of urobilinuria has been suggested as a guide to the functional efficiency of the liver, but it is an unreliable one, as the excretion of the substance fluctuates considerably from day to day and is influenced by factors other than the condition of the liver and the rate of hemolysis.

Urobilin is excreted in the urine only in the form of its chromogen, urobilinogen, which upon exposure to the air quickly oxidizes to urobilin.

## CYSTINURIA

Cystin is a sulphur-containing amino-acid. Normal urine may contain a trace of it. *Cystinuria* is a rare anomaly of metabolism in which the urine contains considerable, often large, amounts of cystin. Of 175 cases collected

[1] Arch. Int. Med., Feb., 1914.

from the literature by Hofmann,[1] 85 were in males and 45 in females. The condition is often congenital and may occur in families for several generations. The cystin is formed in the tissues, not in the alimentary tract, and the amount in the urine is independent of the diet. Indeed, cystin itself, administered by the mouth, does not intensify the cystinuria. In the urinary sediment cystin appears as colorless, highly refractive hexagonal plates, which are readily soluble in ammonia or hydrochloric acid, but which are insoluble in acetic acid. Being rich in sulphur, it imparts to decomposing urine the odor of sulphuretted hydrogen. In some cases the cystin is accompanied by the diamins, cadaverin and putrescin, and also by leucin and tyrosin.

Cystinuria usually continues throughout life. The anomaly of metabolism does not appear to influence deleteriously the general health, but it sometimes leads to the formation of renal or vesical calculi. Rovsing[2] observed 2 cases of cystin stones in 533 cases of nephrolithiasis. No effective treatment of cystinuria is known.

## ALKAPTONURIA

The name alkaptonuria is applied to a condition first described by Boedeker in 1859, in which the urine turns black on standing or on the addition of alkalies. The change of color is due, as Baumann and Wolkow[3] subsequently demonstrated, to the presence of homogentisic acid (dioxyphenyl-acetic acid), which is a normal intermediary substance in the catabolism of tyrosin and phenylalanin, the individual with alkaptonuria being unable to break down these amino-acid units of the proteins to their end products. Urine containing alkapton reduces Fehling's solution, but yields negative results with the bismuth test for sugar and does not ferment. Alkaptonuria is due to a rare anomaly of metabolism analogous to that causing cystinuria. It is frequently observed in several members of one family. Of 40 cases collected by Garrod[4] 29 were in males and 11 in females. It is usually congenital and persists throughout life. The general health does not suffer, but a blackish discoloration of the cartilages and even of the scleræ and skin—*ochronosis*—develops in some cases. Of 32 cases of ochronosis analyzed by Poulsen,[5] in 17 there was alkaptonuria, in 8 phenol dressings had been used for long periods, and in 7 the cause of the discoloration was not apparent.

## PHOSPHATURIA

Phosphoric acid is present in the urine in the form of the *alkaline* phosphates (phosphates of sodium and potassium) and the *earthy* phosphates (phosphates of calcium and magnesium). The alkaline phosphates being very soluble in either acid or alkaline urine are not met with as urinary deposits. In acid urine the earthy phosphates are also held in solution, but in alkaline urine they are precipitated in the form of an amorphous white sediment, which is made more marked by the application of heat. When the urine becomes ammoniacal from decomposition, the ammonia combines with the magnesium phosphate to form ammoniomagnesium phosphate, a so-called *triple phosphate*. This occurs in two forms—triangular prisms with beveled ends (coffin-lid crystals) and, less frequently, stellate or fern-shaped crystals.

[1] Cent. Grenz. Med. u. Chirurg., 1907, 721.
[2] Hospitalstidende, 1919, No. 1.
[3] Zeitsch. f. physiol. Chem. vol. xv, 1891
[4] Lancet, Dec. 13, 1902.
[5] Münch. med. Woch., 1912, lix, 364.

In urine that is feebly acid and tending to ammoniacal change, calcium phosphate may also assume a crystalline form, appearing as small white rods, either singly or in fan-shaped clusters.

The phosphates of the urine are derived chiefly from the food, but partly from the tissues. Normally, from 3 to 4 grams are excreted in the urine daily. A sediment of earthy phosphates in the urine is not in itself evidence of an increased excretion of phosphates. More frequently, it is merely an indication of diminished urinary acidity. True phosphaturia can be determined only by quantitative analysis. Phosphatic precipitates occur when the diet is rich in vegetables (alkaline salts), when alkalis are given repeatedly in large doses, when there is a marked loss of acid from the body, as in some cases of hyperchlorhydria, and in certain digestive disturbances, when the normal excretion of calcium by the colon is much decreased and that by the kidneys is correspondingly increased. An increase of urinary phosphates may also be observed in febrile infections, in leukemia, in diabetes mellitus and other wasting diseases and, for reasons unknown, in certain neurasthenic states. Finally, Tessier[1] and other French clinicians have described under the name of *phosphatic diabetes* an obscure disturbance of metabolism characterized by an excessive output of phosphates in the urine.

Deposits of amorphous phosphates rarely form concretions, but calculi of uric acid and of calcium oxalate are frequently encrusted with ammonio-magnesium phosphate that has been produced as a result of cystitis.

## OXALURIA

The term oxaluria is used to designate the excessive excretion of oxalic acid in the urine. Normally, the daily output is about 0.02 gm. The source of the oxalic acid in the urine is still in dispute. A portion is undoubtedly derived from food-stuffs containing preformed oxalic acid, such as spinach, rhubarb, tomatoes, sorrel, cabbages, grapes, etc. Another portion is probably produced in the alimentary canal by the action of bacteria on carbohydrates and certain amino-acids. A third portion may be formed in the tissues (endogenous oxalic acid) from glycuronic acid, glycocoll, creatin, and even uric acid.

Owing to its strong affinity for calcium, oxalic acid appears in the urine in the form of calcium oxalate. As the latter is soluble in urine in proportion to the quantity of acid phosphates it follows that a precipitation of calcium oxalate crystals does not necessarily indicate an excess of oxalic acid. True oxaluria can be determined positively only by quantitative urinalysis, although its existence may be surmised when the crystals are abundant and are present for a considerable period. Crystals of calcium oxalate occur as colorless, highly refractive octahedra or dumb-bell shaped formations, which are soluble in hydrochloric acid, but are unaffected by acetic acid.

Oxaluria can no longer be regarded as a special disease. In many cases it is dependent upon intestinal fermentation. In other instances it is solely the result of the ingestion of foods rich in oxalates. It is also observed at times in diabetes, gout, leukemia and other diseases in which there are disturbances of metabolism or digestion.

## PNEUMATURIA

Pneumaturia, or the passage of gas bubbles with the urine, is a rare phenomenon. It may be due to the presence of a fistulous communication

[1] Thèse de Paris, 1877.

between the bowel and the bladder, but more frequently it depends upon the production of gas in the bladder by bacteria, usually colon bacilli. Most of the cases have occurred in association with glycosuria, fermentation of the sugar in the bladder resulting in the formation of large quantities of carbon dioxid. Adrian and Hamm[1] have reported a few cases in which glycosuria was absent and the gas was apparently formed by the bacterial decomposition of albumin.

## MOVABLE KIDNEY

**(Floating Kidney; Wandering Kidney; Nephroptosis)**

Normally the kidneys possess a very slight range of motion, and when the abdominal walls are thin and relaxed the lower border of the right one is frequently palpable. When the mobility of the organ is increased, but not to a great extent, the condition is known as *movable kidney*, and when the organ is so freely movable that it forms a definite abdominal tumor the condition is termed *floating kidney*.

Although there is much diversity of opinion as to the frequency of the lesion, all authorities agree that it is much more common in women than in men, that it occurs most frequently between the ages of 25 and 50 years and that it is rare in children. In 1315 patients, 772 men and 543 women, Einhorn[2] found 126 movable kidneys; 14, or 1.8 per cent. among the male patients and 112, or 20.6 per cent. among the female patients. In the large majority of cases it is the right kidney that is affected; sometimes the condition is bilateral, and very rarely the left kidney alone is movable.

The occurrence of movable or floating kidney is favored by a number of factors. One of the most important of these, as Wolkow and Delitzin[3] have pointed out, appears to be abnormal shallowness, congenital or acquired, of the paravertebral fossæ. Compression of the waist by tight lacing or heavy skirts, faulty posture, relaxation of the abdominal walls as the result of repeated pregnancies or the removal of large abdominal tumors, and a lack or loss of the perirenal fat may be regarded as predisposing causes. Direct or indirect violence appears to play a part in some instances; it is probable, however, that traumatism is more potent in dislocating a kidney that is already movable than in imparting mobility to one normally fixed. The frequent more involvement of the right kidney is chiefly due, no doubt, to the impact of the liver during respiration, but the support afforded the left kidney by the descending colon and the greater thickness of the peritoneal folds on the left side (Gerota) are also factors.

**Symptoms.**—The following method of examination will usually serve to reveal the condition. The patient is placed in the dorsal position with the thighs and legs extended and the feet slightly elevated. The examiner's left hand is pressed against the lumbar region so as to push the kidney forward, while the right hand is firmly applied to the abdominal wall. The patient is then directed to take a deep breath, when the kidney, if loose, will be felt as a smooth, round body, with more or less mobility. Sometimes the examination is better performed while the patient is in the knee-elbow position or is standing and bending slightly forward with the hands resting upon a table.

[1] Mitteil. grenzgeb. der Med. u Chirurg., 1907, xvii, p. 10.
[2] Medical Record, Aug. 13, 1898.
[3] Die Wanderniere, Berlin, 1899.

When the kidney is freely movable and completely dislocated it is frequently possible to palpate the entire viscus, which may then be recognized by its size, consistence, and slippery feel, the absence of pain or the occurrence of a dull, sickening ache on pressure, the possibility of replacment, and very rarely, the pulsation of the renal artery. Occasionally, inspection reveals flattening, and percussion a lack of resistance in the lumbar region of the affected side.

In many cases there are no subjective symptoms. Sometimes certain nervous or gastrointestinal phenomena are present, but they are in no way related to the renal abnormality. In other cases movable kidney itself is directly or indirectly responsible for a variety of disturbances. As a rule, the latter include local discomfort, derangement of digestion, and the general phenomena of neurasthenia. The symptoms are usually more pronounced during menstruation and are aggravated by walking or standing. The degree of discomfort varies from a sense of dragging or dull aching to acute lancinating pain. In some cases the pain is referred to the region of the appendix or ovary rather than to that of the kidney. Irritability of the bladder is common. Not rarely temporary hydronephrosis develops from kinking of the ureter. If the latter occurs suddenly, with twisting of the renal vessels, there may be severe pain with nausea, cold sweats, scanty urination, and even hematuria (Dietl's crises[1]), as in attacks of calculus colic. Eventually, hydronephrosis may become permanent.

The digestive disturbances are not characteristic. Patients frequently complain of anorexia, distress after eating, flatulence, palpitation and constipation. In many cases there are signs of gastroptosis, of enteroptosis, or of the so-called "*cecum mobile*" of Wilms. Indeed, the drag on the right kidney of an ascending colon that has suffered prolapse, owing to a defect in its supporting attachment, is regarded by some authorities (Coffey, Goldthwait, Longyear) as an important cause of nephroptosis. Occasionally, there are attacks of persistent vomiting and very rarely there is periodic jaundice, with or without colic, from traction on the duodenum. A floating kidney is more prone than a fixed one to infection, consequently attacks of pyelonephritis are not uncommon.

Nervous symptoms, if not present merely as a coincidence, are usually an effect of the constant nagging discomfort in the abdomen. In some cases, however, they are due to solely to worry occasioned by a knowledge of the fact that an anomaly exists. For this reason patients' attention should not be drawn to the condition unless there is very good reason for believing that it is the cause of their symptoms.

**Diagnosis.**—The diagnosis can usually be made without much difficulty, but the condition may be confused with tumor of the gall-bladder, pylorus, omentum, intestine or ovary, nephrolithiasis and chronic appendicitis. Before rendering a definite decision all the evidence obtainable from the history, subjective symptoms and physical signs should be given the most careful consideration. In doubtful cases recourse may be had to x-ray studies of the kidney after its pelvis has been filled with an opaque medium, such as a solution of sodium bromid or of thorium nitrate. This method reveals displacement of the organ and shows whether or not there is any hydronephrosis.

**Prognosis.**—Life is seldom endangered by movable kidney, but the symptoms often prove obstinate. In many cases, however, we may hope for marked improvement, if not actual recovery, even without operation. Sometimes the symptoms abate spontaneously in advanced age.

[1] Wien. med. Woch., 1864, Nos. 36 and 37.

**Treatment.**—Treatment is required only when the renal mobility is causing definite symptoms. In cases with symptoms relief is frequently secured by the use of a snugly-fitting abdominal binder. In floating or wandering kidney it is usually necessary to employ a suitable pad in addition to the binder. The latter should be made of stiff material and should be large enough to envelop the entire abdomen. The corset constructed by Gallant[1] and designed to make upward and backward pressure is usually effective. The pad should be about 3 inches (7.5 cm.) long, 2½ inches (6.5 cm.) wide, half an inch (1.25 cm.) thick at the upper border and an inch and half (3.75 cm.) thick at the lower border, and so placed that the upper border faces upward and slightly toward the right. Whatever support is used it should always be applied while the patient is recumbent with the buttocks elevated and the kidney is in place.

Patients with nephroptosis should be advised to avoid sudden muscular efforts and to rest during menstruation. General hygienic measures and cautiously practised exercises intended to improve the tone of the abdominal muscles are to be recommended. In neurasthenic women the "rest cure" often yields excellent results. When pain is sufficiently severe to impair the working efficiency of the patient and palliative measures prove ineffective, surgical treatment, usually nephropexy, is indicated. Operation, when applied with judgment and properly performed, is successful in the large majority of cases. The least amenable to surgical treatment are the cases associated with general visceroptosis. Nephropexy should rarely be undertaken merely for the relief of nervous symptoms, as experience has taught that it not only fails, as a rule, but may render the state of the patient worse.

## CONGENITAL ABNORMALITIES OF THE KIDNEYS

The most common congenital abnormalities are rudimentary development or complete absence of one kidney, fusion of the two kidneys, usually with formation of the horseshoe kidney, congenital misplacement of the kidneys (renal ectopia), preservation of the lobulation existing in fetal life and early infancy, and cystic kidneys (see p. 796). Somewhat frequent also are anomalies of the ureters (usually double ureter) and of the blood vessels. Supernumerary kidneys may be observed, but are rare.

From 13,500 postmortem examinations R. Thompson[2] collected 23 cases of solitary kidney, or 1 in 587 autopsies. In contemplated operation on one kidney, especially nephrectomy, the presence and the functional capacity of the other kidney should be determined by palpation, cystoscopy, and ureteral catheterization with chemical tests (see p. 763). The discovery of two ureteral orifices on cystoscopic examination is not absolute proof that two kidneys are present, as in rare instances two ureters have been found issuing from a single large kidney.

The frequency of congenital misplacement of the kidney has been variously stated. Naumann has reported 21 cases in 10,177 autopsies and Guizzetti and Pariset 18 cases in 20,000 autopsies. The ectopic organ, which is the left more frequently than the right, is usually located in the pelvis and is, as a rule, firmly fixed. Genital malformations are also present in many cases. The affected kidney may be sound, but not rarely it is the seat of hydronephrosis, cystic degeneration, or concretions. The diagnosis may

[1] Amer. Jour. Obstet., July, 1901.
[2] Brit. Med. Jour., Mar. 1, 1913.

be difficult. It depends on the discovery of a fixed tumor by palpation through the abdominal wall or rectum and the results of cystoscopic examination (pulsation of the renal artery in the trigone) and of x-ray studies, especially pyelography. In doubtful cases the presence of genital malformations is suggestive. The condition is likely to be confused with ovarian cyst, pyosalpinx, and appendicitis.

## CIRCULATORY DISTURBANCES OF THE KIDNEYS

### ACTIVE HYPEREMIA

Active hyperemia of the kidneys is present in the early stages of acute nephritis, hence the acute infectious diseases and the taking in excess of certain drugs, such as cantharides, oil of turpentine, copaiba, etc. are important etiologic factors. It is probably present also in diabetes insipidus. Possibly a sudden constriction of the peripheral blood vessels induced by chilling of the skin may occasionally produce it. Active hyperemia of one kidney occurs when the functional activity of the other kidney is suppressed for any length of time or the other kidney is removed.

**Anatomically,** the kidney is slightly enlarged and of a reddish-brown color. The capsule strips easily. Microscopic examination shows distention of the capillaries and larger vessels and frequently minute hemorrhagic extravasations. Pure hyperemia without any inflammatory or degenerative changes in the parenchymatous tissue of the kidney is rarely observed.

**Clinically,** active hyperemia of the kidneys is important only when it results from infection, poisons or exposure to cold, and whether due to one or another of these causes it can scarcely be distinguished from the milder forms of acute nephritis. The urine is reduced in amount, of high color and of increased specific gravity. It contains a small amount of albumin, erythrocytes and a few casts. In severe cases there may be gross hematuria. The **treatment** is that of acute nephritis.

### PASSIVE HYPEREMIA

Passive hyperemia of the kidneys is most frequently due to chronic diseases of the heart or lungs which impede the venous circulation. More rarely it results from compression or thrombotic occlusion of the renal veins or of the inferior vena cava above the entrance of the renal veins. In the earlier stages the kidney is swollen, dark in color, smooth and firm. The capsule strips readily and on section of the kidney the Malpighian bodies are distinct and the pyramids dark red. Microscopic examination reveals overfilling of the veins and capillaries, and sometimes minute hemorrhagic extravastions. In long-standing cases the kidney is often somewhat smaller than normal, hard, and pigmented (*cyanotic induration*). The capsule may be adherent in places, and the surface slightly granular. Microscopic examination at this stage shows thickening of the walls of the bloodvessels, especially the veins, hyperplasia of the interstitial connective tissue, compression of the tubules, and varying degrees of degenerative change in the tubular epithelium.

**Symptoms.**—The urine is diminished in quantity, is dark in color, and is of high specific gravity (1020–1030). On standing it deposits a reddish sediment of urates. It contains a small amount of albumin, a few hyaline or granular tube-casts and a few blood cells. Symptoms of the primary disease

which has caused the venous stasis (dyspnea, indigestion, enlargement of the liver, edema, etc.) are present. The 'phthalein output is usually low, sometimes under 30 per cent., but in uncomplicated cases there is little or no nitrogen retention, the blood urea remaining about normal. In cases of myocardial insufficiency with general venous congestion it may be inferred that the renal hyperemia is accompanied by a greater or less degree of actual nephritis if there is pronounced hypertension, if the non-protein nitrogen of the blood is increased, and if rest and the administration of digitalis and diuretics of the caffein type fail to produce any definite improvement.

The **treatment** is largely that of the primary condition. Dry or wet cupping in the lumbar region may be of service. Digitalis alone or in combination with caffein, theobromin or theocin is often useful. Mercurial and saline laxatives are usually indicated.

### INFARCTION OF THE KIDNEY

Endocarditis of the left side of the heart, atheroma of the aorta and aortic aneurysm frequently give rise to embolism in the branches of the renal arteries. As these vessels are end-arteries the occlusion usually results in anemic or hemorrhagic infarction, especially the former. In many cases no symptoms mark the occurrence of this complication, but occasionally it is indicated by hematuria and pain in the region of the kidney.

### ANEURYSM OF THE RENAL ARTERY

Aneurysm of the renal artery is a rare lesion. Ziegler[1] in 1903 collected 19 cases of traumatic and 7 of non-traumatic origin. In the latter, embolism or atheroma of the vessels is accepted as the cause. The most important symptoms are tumor and hematuria. These were present in most of the cases. Pain is inconstant. Occasionally it is excruciating. Pulsation and bruit are usually absent. Hemorrhage is the most frequent cause of death. The diagnosis is rarely possible without an exploratory operation. The only hope of saving life lies in nephrectomy. Several cases thus treated ended in recovery.

## NEPHRITIS

**Classification.**—Disease of the kidneys affecting diffusely both organs and characterized by inflammatory lesions of a non-suppurative character or by simple degenerative alterations has long been known as *Bright's disease.* This name has been associated with such renal changes because Richard Bright, of Guy's Hospital, London, in 1827 first drew attention to their frequency and pointed out their relations both to albuminuria and to dropsy. While different types of the disease are universally recognized, there is as yet no general agreement concerning the definition of the different types. The study is especially complex because in the majority of cases we are still ignorant of the precise causes of the various renal changes; because the appearance of the kidneys at autopsy represents only one stage of a process that must necessarily produce according to its duration a great variety of pathologic pictures, and because up to the present it has been impossible to correlate, except in a very general way, the functional disturbances with the

[1] Centralblatt f. d. Grenzebiete d. Med. u. Chir., vi, 1903.

anatomical findings. Wilks'[1] studies led him to believe that under the name of Bright's disease there are included at least two independent affections—"the large, white kidney with considerable dropsy," and "the hard, contracted kidney, often destitute of symptoms." Later, Virchow proposed the terms *parenchymatous nephritis* and *interstitial nephritis*, for these two conditions, suggesting that in the large white kidney the tubular epithelium, and in the hard contracted kidney the interstitial tissue, was mainly affected. While this division of Wilks and Virchow is a simple one and still has its advocates, it unfortunately has failed to harmonize the clinical and anatomical findings.

Recent histological studies of non-suppurative nephritis have shown that there are at least three groups of cases. In one group degeneration of the tubular epithelium is the principal feature, the glomeruli and the interstitial tissue being much less or not at all involved. In the second group the lesions are found chiefly in and about the Malpighian tufts, and are of an inflammatory and degenerative nature. The process may be diffuse and affect virtually all of the tufts or it may be focal and confined to certain tufts here and there throughout the organ. In the third group the conspicuous alterations are an increase of fibrous connective tissue around the glomeruli and between the tubules and sclerosis of the smaller bloodvessels, although many of the glomeruli show hyaline degeneration or are obliterated and many of the tubules present atrophic changes. The form of renal disease in which the tubular epithelium is chiefly involved is usually termed *tubular nephritis*, and the form in which the glomeruli are mainly involved is known as *glomerulonephritis*. Overlapping is very common in these two types, and in many cases it is difficult to decide from either the clinical or the anatomical picture whether a case is primarily one of tubular or of glomerulonephritis. The tubules are always eventually injured by destruction of the glomeruli and vice versa, and it is probable that in some instances an injurious agent or a combination of such agents acts simultaneously upon both tubules and glomeruli. A case combining the characteristics of both tubular and glomerulonephritis may be classed as one of diffuse nephritis.

That form of kidney disease in which the most conspicuous anatomical change is an overgrowth of cicatricial fibrous tissue around the glomeruli and between the tubules is best termed *renal sclerosis*, although it is usually referred to as chronic interstitial nephritis. Renal sclerosis is always an end-stage of some earlier process affecting the kidneys. In some cases it represents the last stage of glomerulonephritis or of diffuse nephritis, a relative or perhaps an actual increase of connective tissue appearing in the organ as the parenchyma disappears (secondary contracted kidney). More frequently renal sclerosis is the result of a general arteriosclerosis in which the smaller arterioles especially are affected (primary arteriosclerotic contracted kidney). In this condition the renal process is more or less incidental, although the changes in the kidneys are sometimes so extensive that they seriously impair the function of the organs. Occasionally, renal sclerosis develops as a sequel of acute non-suppurative interstitial nephritis, a rare disease, which occurs in the course of severe infections, especially scarlatina or diphtheria, and which is characterized by an extensive infiltration of the renal connective tissue with wandering cells of various sorts, the glomeruli and tubules remaining relatively intact.

For practical purposes the following classification of nephritis, based upon that of Volhard and Fahr[2] may be adopted, although it must always be

[1] Guys' Hosp. Rep., 1853, vol. viii, 2d series.

[2] Volhard and Fahr: Die Brightische Nierenkrankheit, Berlin, 1914.

borne in mind that there are many transitional types which do not fit accurately into any one group:

(A) Tubular Nephritis:
  I. Acute stage.
  II. Chronic stage.
(B) Glomerulonephritis:
  I. Diffuse form,
    1. Acute stage.
    2. Chronic stage.
    3. End-stage (renal sclerosis).
  II. Focal form,
    1. Acute stage.
    2. Chronic stage.
(C) Arteriosclerotic Contracted Kidney.
(D) Septic Interstitial Nephritis.

**Uremia.**—Uremia is a symptom-complex, referable for the most part to the central nervous system, and occurring in diseases of the kidneys when the functional activity of these organs is seriously impaired or resulting from complete anuria induced by ureteral obstruction or other conditions.

Etiology.—Nephritis, acute or chronic, is the disease in which uremia is most likely to occur. Less frequently it is due to obstruction of the ureters by calculi, or is induced by the removal of the only functioning kidney. In chronic nephritis it may develop spontaneously as a result of the structural changes in the kidneys themselves, although in many instances it is directly traceable to some extrarenal factor that has temporarily increased the functional insufficiency of the damaged kidneys, such as an intercurrent infection, pregnancy, a debauch, cardiac incompetence, chilling of the body, trauma, or intemperance in eating.

Symptoms.—The symptoms are variable and depend to some extent upon the nature of the causative lesion. Acute and chronic forms are recognized, although no sharp line can be drawn between them. In the acute form the onset is sudden and the symptoms are, as a rule, stormy; in the chronic form the onset is gradual and the symptoms are more or less subdued until near the end.

Uremia resulting from complete anuria is characterized by anorexia, progressive weakness, increasing stupor, and finally, death within a few days. Evidences of irritation of the cerebral motor centers, such as epileptiform convulsions, are wanting and marked gastric disturbances, other than absolute anorexia, are uncommon. This so-called *asthenic type* of uremia occurs when both ureters are completely obstructed, after removal of the only kidney, not infrequently in mercuric chlorid poisoning, and occasionally in chronic nephritis when intense engorgement of the kidneys occurs as a result of acute cardiac insufficiency.

Uremia developing in the course of ordinary nephritis may be characterized by disturbances of the nervous system, of the digestive organs, or of the respiration. General convulsions, followed by coma, are among the most common manifestations, and hence the term *eclamptic* has been applied to this type of uremia. The convulsive seizures, which closely resemble those of true epilepsy, may occur abruptly and even unexpectedly, but as a rule they are preceded for days or weeks by symptoms of chronic uremia, such as headache, vertigo, drowsiness or wakefulness, dimness of vision, anorexia and a sense of exhaustion. In some cases the convulsive attacks are incomplete, being scarcely more than muscular twitchings; in other cases they are

confined to one member or to one-half of the body, as in Jacksonian epilepsy. Not rarely coma develops without the occurrence of epileptiform seizures and continues uninterruptedly or with slight remissions for several days. In this condition the temperature is usually subnormal, although occasionally there is slight pyrexia. Sudden amaurosis is another manifestation. This usually follows convulsions, but it may occur without them. As a rule, the blindness is complete and of short duration (two or three days). It is probably of central origin, as the ophthalmoscopic picture is often negative or merely that of slight retinal edema. Loss of hearing has also been noted, but it is rare. Occasionally motor paralysis is an important feature. Although, it is generally preceded by convulsions, it may be the only conspicuous expression of the uremic state. Hemiplegia and brachial monoplegia are the most common types. The paralysis is often transitory, and has a marked tendency to recur. When right-sided it is not rarely associated with motor aphasia. The latter may also occur as an independent symptom; thus there was no other paralysis in 15 of 29 cases of uremic aphasia analyzed by Riesman.[1] Uremic palsies have been attributed to edema of the brain, but as this condition is not invariably found at autopsy, it is not improbable that in some cases they are due, like the convulsions, to the action of toxins on the motor centers. Weisenberg[2] has described definite alterations in the cells of the paracentral lobule, on the side opposite the paralysis.

Mental disturbances are not very uncommon. They usually follow convulsions and take the form of a mild delirium. Occasionally, however, a true psychosis supervenes without convulsions. In these cases the mental state varies between acute mania, lasting several days, and chronic delusional insanity with hallucinations of sight and hearing, lasting many months. Vomiting and diarrhea are the most characteristic gastrointestinal symptoms of acute uremia. Both of these disturbances have been attributed to the irritant action of ammonium carbonate, a decomposition-product of urea, which may be vicariously excreted by the stomach and bowel. In many cases, however, the vomiting is probably of cerebral origin. The intestinal irritation is sometimes associated with tenesmus and bloody stools. In such cases the autopsy may reveal the lesions of membranous enteritis. Ulceration of the bowel, especially of the colon or lower ileum, has also been repeatedly observed (Rosenstein, Dickenson, Mathieu and Roux, Barie and Delaunay). Occasionally, persistent hiccough is a conspicuous symptom.

The manifestations of chronic uremia often develop so insidiously and are so varied that their true significance is likely to be overlooked. Headache and vertigo are among the most frequent manifestations. The headache may be persistent or it may occur in paroxysms of great severity. Explosive headaches with vomiting in persons who have not been subject to ordinary migraine should always arouse suspicion of renal insufficiency. Disturbances of respiration are also common. Dyspnea may be more or less constant or paroxysmal. The paroxysmal form, which is prone to occur at night, is frequently spoken of as uremic asthma, although it is probable that such suffocative attacks are more frequently dependent upon associated cardiovascular lesions than upon uremic intoxication. Again, the type of breathing known as Cheyne-Stokes respiration may supervene. This phenomenon is usually associated with stupor or coma; sometimes, however, it develops while the patient is up and about. Although always of serious import, it does not invariably signify impending death, and occasionally after persisting for weeks, it gradually disappears. Finally, the breath often has a peculiar ammoniacal odor.

[1] Jour. Amer. Med. Assoc., Oct. 11, 1902.
[2] Proc. Path. Soc., Phila., Feb., 1904.

In many cases indigestion, with anorexia and occasional attacks of vomiting, is an important feature. The tongue is usually coated and the mouth dry. On the other hand, there may be slight ptyalism. Not rarely there are painful cramps in the calves of the legs and occasionally intolerable itching of the skin occurs in association with other manifestations or develops as an isolated symptom. Very rarely a deposit of urea in the form of fine crystals appears on the skin. Especially interest attaches to the actual lesions of the skin that may occur in the course of nephritis. These usually take the form of simple erythema, papular eczema, or urticaria, but in rare instances the final stage has been marked by general exfoliative dermatitis.

The excretion of urine is usually, but by no means invariably, diminished in uremia. The output of urinary solids is almost always diminished (hyposthenuria), even though the quantity of urine is normal or increased. As a general rule, but with some exceptions, the noncoagulable nitrogen of the blood is increased from the normal of 25 to 40 mg. per 100 mils. to 50, 100, 200 or even 300 mg. In asthenic uremia the urea nitrogen in the blood is rarely less than 100 mg. per 100 mils.

Among other nitrogenous constituents, the uric acid is increased from a normal of 1 to 3 mg. to 5 to 10 mg. or more, and the creatinin from 0.1 to 0.8 mg. to 2 to 40 mg. As the blood contains an excess of organic molecules its freezing point is lowered. Recent investigations have shown that acidosis is also frequently present and, while apparently not responsible for uremia, that it may produce somewhat similar symptoms. An increase in the number of leucocytes in the blood is often observed.

Diagnosis.—In the absence of the clinical history, it is sometimes extremely difficult to distinguish between uremia and other conditions causing coma or convulsions. The recognition of nephritis does not render positive the diagnosis of uremia, since cerebral hemorrhage is also common in nephritis. The coma of *cerebral hemorrhage*, however, usually develops more abruptly, and is far more frequently accompanied by complete hemiplegia than that of uremia. Conjugate deviation and a sharp fall of temperature followed within a few hours by a distinct rise are strongly indicative of apoplexy, while an ammoniacal odor of the breath suggests uremia. In a doubtful case a marked increase in the nonprotein nitrogen of the blood would be very important evidence in favor of uremia. The state of the pupils and pulse affords no help in the diagnosis. It is often impossible to form an immediate diagnosis in cases of uremic palsy.

Uremia is at times confused with *acute alcoholism* and *opium poisoning*. Alcoholic coma, as a rule, is not so profound as that of uremia. The odor of alcohol on the breath is doubtful evidence; its absence, however, usually excludes alcoholic poisoning. Minutely contracted pupils point to opium poisoning. The presence of albumin and casts in the urine and high arterial tension render the diagnosis of uremia probable, but not certain, since a patient may have nephritis, and yet be suffering from an excess of one or the other of the two poisons.

*Diabetic coma* may usually be distinguished from uremia by the presence of sugar and diacetic acid in the urine and the peculiar fruity odor of the breath. The differential diagnosis between uremic stupor and that of *typhoid fever* or *meningitis* must be made by the aggregate of symptoms.

The manifestations of chronic uremia are so protean and so easily misinterpreted that the urine of all patients should be carefully studied, otherwise errors in diagnosis must frequently occur. In doubtful cases an examination of the eye-ground and a determination of the amount of nonproteinni trogen of the blood should also be made. The close resemblance

that mild uremic intoxication may bear to *neurasthenia* must constantly be borne in mind.

PATHOGENESIS.—This is obscure. The kidneys being the chief organs for the excretion of the products of nitrogenous metabolism, it is a natural conclusion that uremia is a result of the retention of these products in the blood. As a matter of fact, high figures for the residual or non-protein nitrogen of the blood are usually observed in uremics. Nevertheless no known constituent of the urine seems to be capable of producing all the phenomena of the syndrome. However, Hewlett, Gilbert and Wickett[1] have recently shown that when urea is administered to normal persons in such amounts that the concentration of this substance in the blood reaches 160 mg. per 100 c.c., or about the concentration, usually observed in spontaneous uremia, symptoms comparable to those of asthenic uremia gradually develop. On the other hand, it is definitely known that uremia, especially that type in which epileptiform seizures are a conspicuous feature, may occur when the urea and total incoagulable nitrogen of the blood are not increased. This fact, together with the observation that complete suppression of urine through mechanical obstruction of both ureters, is not followed by convulsions or other irritative cerebral phenomena, suggests that the various manifestations of uremia do not depend upon a single cause, and that at least one form of the syndrome, that, in which epileptiform convulsions dominate the clinical picture, may be due not to the retention in the body of any normal urinary substance, but to a poison produced by a wholly abnormal type of metabolism. Recently, Foster[2] has reported the finding of a crystalline substance in the blood of convulsive uremics which in animals produces the symptoms of the eclamptic type of uremia and finally death, and which cannot be detected in normal blood or in blood in any diseased state except uremia of this type. If this observation should be confirmed it would strongly support the contention that in the convulsive form of uremia there is an abnormal metabolism, as well as nitrogen retention.

In view of all the facts, therefore, it seems highly probable that the varied symptoms of uremia do not all arise from a common cause, but that in one group of cases (asthenic) urea is an important factor, and in another group (eclamptic) some poison resulting from abnormal metabolism plays the chief rôle. Possibly, as Foster and others have suggested, there is a third group of cases, characterized by vomiting, headache, amaurosis, and coma, in which cerebral edema, the result of water and salt retention, is the disturbing influence, for when lumbar puncture is done in these cases the cerebrospinal fluid is usually found to be under increased pressure and after some of the fluid has been removed there is, as a rule, temporary improvement in the patient's condition. Of course, it must be recognized, that even if these hypotheses are correct, that in very many cases of uremia more than one factor is present, and further, that such complications as acidosis and high blood pressure often add to the complexity of the clinical picture.

**Tests of Renal Functional Capacity.**—Used routinely in conjunction with other procedures renal functional tests are valuable aids to diagnosis, prognosis and treatment in all forms of kidney disease. There are two groups of tests: (1) Those of the excretory capacity through quantitative determinations of the elimination of various substances in the urine, especially certain dyes (phenolsulphonephthalein, indigocarmin, etc.) sodium chlorid and urea; (2) those of retention through quantitative determinations of the concentration of certain substances in the blood, especially incoagulable

[1] Arch. Int. Med., Nov., 1916.
[2] Jour. Amer. Med. Assoc., Sept. 23, 1916.

nitrogen, urea, and creatinin. In all cases the results are more reliable when the tests are made at intervals.

*Phenolsulphonephthalein Test.*—Of the various dyes used to test the excretory capacity of the kidneys, phenolsulphonephthalein ('phthalein) has been shown to be the most satisfactory. A solution is made containing 6 mg. of the dye to 1 mil of salt solution. This is injected into the lumbar muscles under aseptic conditions. Following the injection all the urine excreted is collected at the end of one and two hours, is diluted to a suitable amount with alkaline water and its 'phthalein content is estimated by colorimetry. Normally, from 50 to 75 per cent. of the amount of dye injected is recovered in two hours. In severe chronic nephritis the 'phthalein excretion in 2 hours usually varies from 35 per cent. to 0. In passive congestion of the kidneys, the result of cardiac insufficiency, the eliminaton of 'phthalein, although often considerably reduced, is usually rapidly restored with the re-establishment of compensation A 'phthalein excretion below 30, in patients who present no signs of cardiac insufficiency, indicates usually severe renal lesions. Although uremia may not appear for many months, even if the 'phthalein excretion is virtually nil, provided the amount of blood urea is still comparatively low.

The 'phthalein test, if repeatedly applied, gives a fairly reliable index of the functional capacity of the kidneys, especially in cases of chronic nephritis. It is also of value in affording an indication of the relative integrity of the two kidneys in cases of pronounced unilateral disease if the urine can be obtained separately from each organ.

*Sodium Chlorid Excretion.*—This is usually determined by a quantitative estimation of the intake of salt in the food and the output in the urine. Schlayer has suggested the addition of 10 grams of sodium chlorid at one dose after the patient has reached a salt equilibrium by being on a known diet for several days. Normally, nine-tenths of the added salt should appear in the urine within 48 hours. Salt retention is of little prognostic significance, but it may be useful in making an early diagnosis of chronic nephritis, as it is often present when the kidneys are still able to excrete phenolsulphonephthalein and other dyes. It bears no direct relation to the degree of nitrogen retention, or to the development of uremia, but it is usually accompanied by edema.

*Urea Excretion.*—In the early stages of nephritis the excretion of urea is usually normal, but as the lesions increase in severity there is, as a rule, a steady decline in excretion, and upon the approach of uremia there may be complete retention. Monakow has suggested the administration of 20 grams of urea at one dose after the patient has been on a known diet for several days and his urea excretion has become virtually constant. Normally, this excess of urea is wholly excreted within 48 hours. The estimation of the urea nitrogen of the urine is of little help in making an early diagnosis of nephritis and is absolutely valueless when a small quantity of urine taken at random is used for the purpose, but it is decidedly useful for prognosis when made under known conditions of diet and at definite intervals during the seventy-four hours, especially if additional urea be taken with the food as in Monakow's test. It is not advisable, however, to add the urea to the food if the 'phthalein test, which should be made first, shows the renal excretion to be very low.

*Two-hour Test Meal.*—The so-called two-hour test meal, first suggested by Schlayer and Hedinger,[1] and modified by Mosenthal and others in this country, is particularly useful in differentiating degrees of renal involvement in the milder forms of nephritis. By it nocturnal polyuria, fixation of the

[1] Deutsch. Archiv. f. klin. Med., 1914, cxiv, 120.

specific gravity of the urine, and failure of the kidneys to secrete a concentrated urine normally rich in salt and nitrogen are readily detected. Three meals a day (the last at 6 P.M.) are allowed, the aggregate food containing about 13 grams of nitrogen, 8.5 grams of salt, and in 1760 mils of fluid.[1]

The patient should pass urine every two hours from 8 A.M. to 8 P.M. and each portion should be collected in a separate bottle with a label indicating the time of micturition. The urine passed during the 12 night hours may be collected as one specimen. The examination of each of the seven specimens should include the quantity, specific gravity and the percentage of salt and nitrogen. Frequent examinations of the day and night urine, even with the patient on an ordinary mixed diet yield fairly good results. Normally, when no excess of fluid is taken, the specific gravity of the urine at some time of the day reaches 1020 or over and the night urine does not exceed 450 mils

*Nitrogen Retention.*—In healthy adults the total non-protein or non-coagulable nitrogen of the blood ranges between 25 and 40 mg. per 100 mils and the urea nitrogen between 10 and 18 mg. per 100 mils. As a general rule, with some exceptions, the amount increases as the renal impairment becomes more pronounced, the highest figures occurring in uremia in which the concentration of non-protein nitrogen may exceed 250 mg. As a rule, the accumulation of nitrogen in the blood is more pronounced in glomerular than in tubular nephritis. In uncomplicated passive congestion of the kidneys, which may greatly impair the 'phthalein output, there is often no material increase in the blood nitrogen.

Ambard's quotient, or McLean's modification of it, which was formulated to express precisely the relation between the urea concentration of the blood and urine and the rate of urea excretion, is apparently a no more reliable index as to renal involvement or prognosis than the determination of the blood urea alone.

*Creatinin Retention.*—Myers and Killian[2] have recently pointed out that the creatinin in the blood is even a more reliable index of the decrease in the permeability of the kidneys than urea, for the reason that creatinin, when the patient is on a meat-free diet, is entirely endogenous in origin and its formation (and excretion normally) are very constant. According to these observers any values for creatinin above 1 or 2 mg. per 100 mils of blood probably indicate a pathologic condition, figures from 3 to 5 mg. are decidedly unfavorable, while concentration above 5 mg. almost always indicates an early fatal termination. Occasionally creatinin concentration reaches as high as 30 mg. or higher.

## ACUTE NEPHRITIS

**Etiology.**—Acute nephritis is usually caused by some acute infection, scarlet fever, diphtheria, measles, smallpox, influenza, typhoid fever, pneu-

[1] The following meals used at the Peter Bent Brigham Hospital are palatable and give satisfactory results:

*Morning meal:* Orange 50 grams, oatmeal 150 grams and milk 25 c.c.; 1 egg 50 grams, toast 20 grams and butter 5 grams, sugar 10 grams and cream 20 c.c., to be used with 150 c.c. of tea or coffee.

*Mid-day meal:* Milk (in soup) 150 c.c, steak 75 grams, potato 100 grams and butter 10 grams; peas 100 grams and butter 10 grams; bread 20 grams and butter 5 grams; ice cream, composed of milk 100 c.c., cream 20 c.c., sugar 10 grams and 1 egg 50 grams, sugar 10 grams, NaCl 3.5 grams (to be used by patient on above food) and water 500 c.c. with meal.

*Evening meal:* Tomatoes 75 grams and butter 10 grams, lettuce 20 grams with celery 50 grams and olive oil 20 c.c., bread 20 grams and butter 5 grams, baked apple 100 grams with sugar 20 grams and cream 20 c.c., water 500 c.c. with meal. 250 c.c. water during evening.

[2] Amer. Jour. Med. Sci., May, 1919.

monia, cerebrospinal meningitis, cholera, erysipelas and pyococcic infections being especially prone to induce it. Focal infection, particularly when it affects the tonsils, is also an important etiologic factor. Acute syphilis is a relatively uncommon cause, although Munk[1] collected 14 cases in the Kraus Clinic (Berlin) in three years. In these various infections the toxins of the specific organisms may sometimes be responsible for the renal lesions, but doubtless in many instances the bacteria themselves are the injurious agents. Less frequently, acute nephritis is a result of the action of some chemical irritant that is excreted by the kidneys, such as mercuric chlorid, turpentine, phenol, salicylic compounds, ether and cantharides, and in other cases it is due to some metabolic poison brought to the kidneys by the blood; thus, it may be associated with pregnancy, hemoglobinemia, extensive burns, generalized eczema, etc. The kidney of pregnancy must be distinguished from nephritis occurring accidentally in pregnancy as a result of an infection or an exogenous poison. It is observed especially in young primiparæ and during the latter half of pregnancy. It is doubtless of toxic origin, although disturbance of the renal circulation due to the increased intra-abdominal pressure is probably a factor of some importance. Exposure to cold is not rarely responsible for an acute exacerbation of an already existing nephritis, but it is doubtful whether chilling itself is capable of producing the disease.

Scarlet fever, streptococcus infections, particularly infections with streptococcus viridans, and certain poisons, such as cantharides, are especially concerned in the production of acute glomerulonephritis; on the other hand, pregnancy, some of the infections, such as typhoid fever and cholera, and certain mineral poisons, notably mercuric chlorid and the chromates, usually produce an acute tubular nephritis.

**Morbid Anatomy.**—In mild forms of the disease the kidney often presents no conspicuous macroscopic changes, although it is sometimes slightly enlarged and somewhat opaque. In well-developed cases the organ is distinctly swollen, the capsule is tense and strips readily, and the surface is grayish or mottled, buff-colored and reddish areas being intermingled. In glomerulonephritis the tufts often stand out prominently as pale, translucent points. In this form, too, ecchymoses are very common, and occasionally the hemorrhages are so numerous that the entire organ is of deep red color.

Microscopically, the important changes in *glomerulonephritis* are in and about the tufts. A characteristic feature in many cases is the presence of a hyaline thrombus in a circumscribed portion of a capillary loop in a certain number of glomeruli. This thrombus may owe its origin to the action of toxins on the capillary wall, but in some instances it is undoubtedly produced by clumps of bacteria which have become impacted in the affected vessel (Baehr[2]). Many of the capillaries that are not occluded by thrombi are distended with leucocytes. The cavity of the capsule is usually filled with blood or with albuminous material, leucocytes and proliferated and desquamated epithelium. Virtually all the tufts may be affected (diffuse glomerulonephritis) or only a tuft here and there may show evidence of disease (focal glomerulonephritis). The focal form is observed chiefly in connection with streptococcus subacute and chronic endocarditis, but it occurs also in other streptococcus infections. The tissue between the glomeruli and tubules is edematous and infiltrated more or less profusely with wandering cells. The tubular epithelium may be intact or nearly so, although in the majority of cases it shows some degenerative change.

[1] Ztschr. f. inn. Med., 1913, lxviii, Nos. 1 and 2.
[2] Jour. Exper. Med., 1912, xv.

In *acute tubular nephritis* the most characteristic feature, histologically, is the extensive degeneration of the tubular epithelium. According to the stage or intensity of the inflammatory process, the epithelial cells are swollen and granular, fatty, or necrotic and desquamating. Here and there, tubules are distended with detached epithelium, detritus, leucocytes, or casts. The intertubular tissue is usually edematous and the seat of an inflammatory reaction indicated by the presence of wandering cells. The glomeruli may be apparently intact, but not infrequently some of them also show changes of inflammatory character.

**Symptoms.**—The *mode of onset* is variable. In mild forms the urinary changes may be not only the first but the only evidences of the disease. The more severe cases sometimes begin with chilliness or vomiting. In other cases edema is the first symptom to attract attention. Occasionally, the onset is marked by uremic convulsions. The *urine* is almost always scanty, and sometimes there is complete anuria. The urine that is excreted is acid in reaction, more or less turbid, dark in color, and of high specific gravity (1025 to 1035). Blood is frequently present, sometimes in sufficient quantity to be readily seen with the naked eye. Chemical examination reveals a considerable quantity of albumin, usually from 0.5 to 1.5 per cent. The total output of urea and chlorids is, as a rule, decreased, although the percentage of these substances may be increased. The sediment is usually very copious and contains renal epithelium, compound granule cells, cellular detritus, leucocytes, erythrocytes, and numerous tube-casts (chiefly epithelial, granular, and erythrocytic). A bacteriologic examination of the sediment not rarely reveals the causative agent. Owing to the increased concentration of the urine and its high acidity, there may be frequent micturition and even vesical tenesmus.

*Edema* is often present from an early period of the disease. It usually appears first in the eyelids or face, in the hands, about the ankles, or in the scrotum, and from these localities it sometimes spreads until it involves the entire subcutaneous tissue, the serous cavities, and even the lungs. Occasionally it involves the mucous membranes, especially the conjunctiva or that of the larynx. The cause of renal dropsy is obscure. The view commonly held at present is that it depends, on the one hand, upon salt or water retention, and on the other, upon an increased permeability of the capillaries, induced by the poisoning incidental to the nephritis.

Fever is sometimes present, but it may be absent if the condition of which the nephritis is a complication is an afebrile one. A dull aching pain in the region of the kidneys is occasionally experienced. Emaciation is common, although it is often concealed by the edema. Pallor is a conspicuous feature, especially in severe cases, the changes in the blood being those of secondary anemia. Dyspnea sometimes occurs. It may be due to hydrothorax, pulmonary edema, secondary infection of the lungs, or retained toxic metabolic products.

In glomerulonephritis, even in cases of average severity, the blood pressure is frequently raised. Except upon the approach of uremia, however, it is distinctly lower than that usually observed in chronic glomerulonephritis. In severe cases uremia (see p. 760) may supervene at any time, although it does not often occur unless there is marked oliguria. Except in mild forms of the disease, functional tests reveal a decrease in the output of 'phthalein and an accumulation in the blood of urea and of total incoagulable nitrogen. The failure of the kidneys to excrete 'phthalein, however, is not a reliable guide to prognosis in acute nephritis, owing to the marked rapidity with which changes in this respect frequently occur.

**Complications.**—The occurrence of inflammation of the serous membranes, especially of pleuritis and pericarditis, is favored by all forms of nephritis. Pneumonia is not an uncommon complication. Myocarditis and acute dilatation of the heart may occur, but usually these are to be ascribed to the underlying infection or intoxication rather than to the nephritis itself. Some degree of cardiac hypertrophy not rarely supervenes after the disease has become subacute. Retinitis, usually bilateral, sometimes develops, especially in the glomerular form and in the kidney of pregnancy, but it is much less common than in chronic nephritis. It is comparatively rare in children.

**Diagnosis.**—No hard and fast line can be drawn between acute nephritis and *febrile albuminuria*, although the presence of inflammatory changes in the kidneys may usually be assumed if the urine persistently contains a fairly large amount of albumin and many blood cells and casts. The occurrence of edema, of uremic phenomena, or of retinal changes is, of course, definite evidence of nephritis. The differential diagnosis between acute nephritis in kidneys previous sound and an *acute exacerbation of chronic nephritis* must be made from the history and course of the disease rather than from an analysis of the urine. An abrupt onset after the operation of one of the obvious causes of acute nephritis (acute infection, pregnancy, poisoning by a chemical irritant), the complete absence of cardiovascular and retinal changes, and a short course favor the assumption that the process is wholly acute.

It is not always possible to distinguish between *acute glomerulonephritis* and *acute tubular nephritis*, and many transitional cases are observed. Generally speaking, however, the occurrence of scarlet fever or of a streptococcus infection as an antecedent cause, high blood pressure, the presence of considerable blood in the urine, and a distinct tendency to uremia point strongly to glomerulonephritis.

**Prognosis and Terminations.**—The prognosis depends largely upon the severity of the attack and the type of the nephritis, as indicated by the general condition of the patient, the quantity and character of the urine, and the results of functional tests. Mild forms of tubular nephritis usually subside completely with the disappearance of the primary infection or intoxication, although several weeks or months often elapse before the urine becomes entirely free of albumin. In some instances, however, the process gradually lapses into subacute or chronic tubular nephritis. Acute glomerulonephritis may also heal without producing any permanent injury in the kidneys, if the cause is promptly removed, but much more frequently there is only a seemingly complete recovery, the condition passing into a subacute or chronic glomerulonephritis without marked symptoms. In severe cases of either type of nephritis death is not uncommon, the immediate cause of the fatal issue being extensive effusions into the pleura or pericardium, edema of the lungs, uremia or pneumonia. Less frequently the end comes through acute dilatation of the heart or pericarditis. Although uremia is always a grave condition, recovery is possible, even if there are convulsions and coma.

**Treatment.**—It may be possible in some instances to prevent the occurrence of nephritis in acute infections by restricting the diet to bland foods, withholding irritant drugs of all kinds, protecting the body against chilling, promoting the functional activity of the skin and intestines, and supplying sufficient water to dilute the toxins and waste matter that the kidneys must excrete. After the disease has actually developed, the indications are to relieve renal congestion, to reduce the work of the kidneys as much as possible and to combat symptoms that threaten life or produce serious discomfort. Only in cases that are clearly syphilitic is there any treatment that exerts a

specific influence on the disease. In syphilitic nephritis, arsphenamin in doses of 3 gr. (0.2 gm.), once a week, cautiously increasd to 6 gr. (0.4 gm.), often produces marked improvement. Mercury is, as a rule, less safe and less reliable, and should be withheld until the acute symptoms have subsided.

Absolute rest in bed is imperative in all cases and should be continued until the acute manifestations have entirely disappeared. The patient should be well covered, flannel being worn next to the skin, and great care should be taken to prevent chilling of the body.

As a rule, milk is the best food, at least for a time. It may be given alone, although usually it is advantageous to dilute it about one-third with lime-water, barley water, simple carbonated water or Vichy. When the kidneys begin to secrete more freely, cream, thin gruels, rice, milk-toast and fruit juices may be given. Beef-tea and broths must be prohibited, as they have little caloric value and contain creatinin and other waste products which the kidneys have difficulty in excreting.

Sodium chlorid should also be withheld, especially if there is edema. Unless edema is pronounced, however, a liberal amount of water, should be allowed, as it tends to dilute the urine and to wash out cell detritus from the tubules of the kidneys. An agreeable beverage may be prepared by adding a dram (4.0 gm.) of potassium citrate, the juice of a small lemon, and a little sugar to a pint (500 mils) of boiling water and allowing the mixture to stand until cold. During convalescence, bread and butter, baked potatoes, and green vegetables are permissible. The return to meat proteins should be very gradual, the effect on the urine of each addition to the diet being carefully observed.

At the onset of the disease, if there is pain or suppression of urine, dry or wet cupping over the region of the kidneys is of service. Following the cupping, a hot-water bag or flax-seed poultice may be applied. Cantharides, oil of turpentine, or other cutaneous irritants should never be used. The bowels should be made to move two or three times a day, the best cathartic for the purpose usually being a saline or compound jalap powder. For children magnesia or cascara sagrada will be found sufficient. Very active purgation is not indicated unless there is extensive edema or uremia.

Free perspiration is useful in promoting elimination through the skin. It may be secured by means of hot-water baths, hot packs, vapor baths, or hot-air baths. In children hot baths and hot packs are eminently satisfactory, especially if a hot drink is administered at the same time. If the baths alone prove ineffective, their action may be supplemented by the hypodermic administration of pilocarpin in doses of from $\frac{1}{12}$ to $\frac{1}{6}$ gr. (0.005–0.01 gm.), but this drug must be used with caution and only employed when necessary.

Stimulant diuretics, such as squill, caffein, theobromin, etc., are contraindicated, but mild alkaline diuretics, such as the organic salts of potassium, often serve a useful purpose in lessening the acidity of the urine, and in removing from the renal tubules epithelial detritus and plugs of albumin. If the heart shows signs of failing, digitalis may be advantageously combined with the alkali, as in the following formula:

℞. Potassii acetatis..... ℥iii
Infusi digitalis..... f℥iii (90.0 mils.) M.
Sig.—Two teaspoonfuls, well diluted, four times a day.

When there is complete anuria, continuous enteroclysis with water or a 2 per cent. solution of sodium bicarbonate at a temperature of 105° F. (40.5°C.) sometimes aids in reëstablishing renal secretion.

If acute nephritis occurs early in pregnancy the uterus should be emptied

as rapidly as possible; if, however, it does not develop until a late period and there are no serious symptoms (edema, retinitis, accumulation of non-coagulable nitrogen in the blood, etc.) operation may be deferred, the effects of rest, appropriate diet, etc. being carefully observed.

Decapsulation of the kidneys, first suggested by Edebohls[1] in 1901, has occasionally proved a life-saving operation in acute nephritis. It may be considered in cases following acute infection or mercury poisoning if there is persistent anuria and symptoms of uremia are developing, and also in the kidney of pregnany if toxic symptoms continue after the uterus has been emptied. The good effects of the operation are probably due to the relief of tension and extreme congestion.

Certain symptoms, such as extensive edema, vomiting, uremia, and anemia often require special treatment.

*Edema.*—If edema is marked and does not yield to restriction of liquids, removal of salt from the diet, and the purgative, diaphoretic and diuretic remedies that have already been indicated, recourse may be had to puncture of the swollen limbs, to free incision on the inner or outer side of each ankle, or the insertion beneath the skin of Southey's tubes. The last, however, should never be used unless all other measures have been found wanting. Large accumulations in the serous sacs should be removed by paracentesis.

*Vomiting.*—If vomiting is persistent, withdrawal of food for a time is advisable. Pieces of ice may be given to quench thirst. A mixture containing bismuth subcarbonate—10 gr. (0.6 gm.) and diluted hydrocyanic acid—1 min. (0.06 mil) or a powder of cerium oxalate—10 gr. (0.6 gm.) and sodium bicarbonate—5 gr. (0.3 gm.) not rarely affords relief. A mustard plaster over the epigastrium may also be tried.

*Insomnia.*—If insomnia is sufficiently pronounced to demand the use of a somnifacient, preference should be given to bromids, chloralamid, or chloral. Trional, sulphonal and, as a rule, opiates should be avoided.

*Uremia.*—This complication calls for prompt and energetic treatment. The chief indications are to favor elimination of toxic metabolic products through the only available emunctories—the intestines and the skin. The bowels should be opened at once by an active cathartic, such as compound jalap powder—30–40 gr. (2.0–2.5 gm.), or elaterium—1/6 gr. (0.01 gm.), or, if the patient is comatose, croton oil—2–3 drops in olive oil on the back of the tongue. Sweating should be promoted by hot-air or vapor baths. If coma or convulsions occur, or if the blood pressure is very high, venesection should be practised, the removal of from 15 to 20 ounces (450.0–600.0 mils) of blood often having a very salutary effects. In children a few ounces of blood may be abstracted from the lumbar region by means of wet cups. Unless there is marked edema, a volume of physiologic saline solution equal to that of the blood abstracted may be given subcutaneously. Whether venesection is deemed necessary or not, irrigation of the colon with a hot 2 per cent. solution of sodium bicarbonate (105° F.–40.5° C.)may be done with advantage. When stupor and coma develop without convulsions lumbar puncture is sometimes of service. If convulsions are not controlled by venesection and depurative measures, bromids or chloral may be given by the mouth or if necessary by the rectum. If these measures fail, a few whiffs of chloroform may be administered by inhalation or morphin (1/4 gr.–0.016 gm.) may be given hypodermically.

During the treatment of uremia the diet should be restricted to milk.

*Anemia.*—After the acute symptoms have subsided iron may be employed to combat anemia. The solution of iron and ammonium acetate (Basham's

[1] Medical Record, 1901, 690.

mixture) is a favorite preparation, but it is doubtful whether it has any advantages over other non-irritant compounds, such as ferrous carbonate or reduced iron.

*Convalescence.*—It is advisable to keep the patient under observation for many weeks after all symptoms of the disease have disappeared. He should be warmly clad and carefully protected from chilling. While the diet should be liberal, it should be such as will not overtax the kidneys. Over-exertion must be rigidly avoided. The skin and bowels should be kept active, the former by frequent baths and the later by saline aperients, if necessary. If the weather is cold, a temporary change of residence to a warm equable climate will be advantageous.

## CHRONIC TUBULAR NEPHRITIS

**Definition.**—The term chronic tubular nephritis is used to designate a form of chronic renal disease in which the most striking feature, histologically, is a pronounced degeneration of the tubular epithelium. Primary or secondary changes in the glomeruli are often observed, but they are not extensive, and there is always some evidence of new connective-tissue formation about the tubules and glomeruli, but this is also a subordinate feature and does not result in induration and contraction until the process is far advanced. No sharp line can be drawn between acute and chronic tubular nephritis, many intermediate stages being met with in practice.

**Etiology.**—Chronic tubular nephritis may be a sequel of acute tubular nephritis, and in some cases the transition from the one to the other can be traced through its various stages. More frequently the disease develops insidiously and seems to be of a chronic nature from the beginning. Although the etiology of this group is often obscure, it is probable that the ultimate cause is always some irritant, of hematogenous origin, acting repeatedly or continuously over a long period, but not with sufficient intensity or rapidity to cause acute nephritis. Some cases can be definitely traced to chronic focal infection, and others to some chronic general infection, such as syphilis, tuberculosis or malaria. There is some justification for the belief that anaphylaxis, or parenteral protein intoxication (Longcope[1]), and even the excretion of excessive amounts of nitrogenous material over a long period of time, as a result of a high protein diet (Newburgh[2]), may be etiologic factors in some instances. Abuse of alcohol and repeated or prolonged exposure to the inclemencies of the weather are frequently cited as direct causes, but it is doubtful whether these factors of themselves can exert more than a predisposing influence.

The disease is most common between the ages of 20 and 40 years and men are more frequently affected than women.

**Morbid Anatomy.**—The gross appearance of the kidneys varies with the extent of the degenerative changes and the duration of the disease. Unless the process is very far advanced, the kidneys are, as a rule, enlarged, softer than normal, and of a pale yellow or yellowish-white color. The capsule is thin and strips easily and the outer surface is smooth. On section, the cortex is widened and light-colored, while the pyramids are reddish-brown. Kidneys presenting these appearances are usually referred to as *large white kidneys*.

In long standing cases, owing to the complete obliteration of many tubules and glomeruli, and an extensive proliferation of connective tissue, the

[1] Jour. Exper. Med., 1913, xviii.
[2] Arch. Int. Med., Oct., 1919.

kidneys may be reduced in size and firmer than normal. Under these circumstances, the capsule is often thickened and, in places, adherent, the outer surface of the organ slightly granular, and the cortex considerably thinned (so-called *secondarily contracted kidneys*).

*Microscopically*, the most striking feature is the extensive degeneration of the tubular epithelium. The tubules are dilated and many of them are filled with detached and degenerated cells, fat globules, and granular or hyaline tube-casts. In places the epithelial lining may be regenerated, but the new cells are greatly shortened. Changes are observed also in some of the glomeruli, the lining epithelium being fatty, the basement membrane of the capsule thickened, and the capsular space infiltrated with albuminous material and occasionally with degenerated epithelium. The interstitial tissue is edematous and more or less increased, owing to the presence of many spindle-shaped fibroblasts, which have taken the place of the wandering cells that are found in acute nephritis. In cases far advanced (secondarily contracted kidney) many tubules with their corresponding glomeruli are obliterated and their places filled by connective tissue poor in nuclei and rich in fibers.

**Symptoms.**—Not rarely the only evidence of the disease for an indefinite period is the presence in the urine of a small amount of albumin and a few pale granular casts. These slight urinary changes, in the absence of other indications, do not necessarily signify a progressive pathologic process in the kidneys; they may be simply the functional expression of permanent, but stationary, structural damage to the renal tissues produced by some irritant that has long since ceased to act. In some cases the clinical picture is virtually that of the acute nephritis out of which the chronic form has slowly developed. In other cases (and these constitute the majority) the first indication is a gradual failure of health, with indigestion and headache, although these symptoms are frequently passed over and the disease is unsuspected until the occurrence of *edema*. The swelling usually appears first about the eyes or in the legs. As a rule it spreads slowly and at intervals it may entirely disappear. Sooner or later, however, anasarca supervenes, effusion occurs in the serous sacs, and the whole body takes on a bloated appearance. The swelling of the external genitals is often extreme, the prepuce becoming so distended and twisted that urination is made difficult. Some degree of anemia is usually present, although in the majority of cases neither the number of red corpuscles nor the percentage of hemoglobin is reduced as much as the peculiar pallid, often wax-like or doughy, appearance of the skin would indicate. Digestive disturbances are rarely absent. The tongue is pale, flabby, and coated with a yellowish-white fur. The appetite is poor and periodic attacks of nausea and vomiting are not uncommon.

The blood pressure is not often increased and it may be subnormal. The functional capacity of the kidneys, as shown by the various chemical tests (see p. 763), is, as a rule, but little impaired. The eye-grounds usually remain normal. Uremia sometimes develops toward the end, but many cases, probably the majority, run their entire course without it.

The *urine* is diminished in quantity, cloudy, of high specific gravity, (1018–1025) and acid in reaction. It contains a considerable quantity of albumin, in some cases as much as 3 per cent. (½ to ¾ by bulk). The sediment is abundant and consists of many hyaline, granular, fatty and epithelial casts, fat droplets, cellular detritus, and leucocytes, but usually few or no erythrocytes.

The active symptoms of the disease may be continuous or nearly so, but

in a large proportion of cases they come on in attacks which last for weeks or months. Between the attacks the patient may be comparatively well, although the urine always contains albumin and casts.

**Complications.**—Most of these are due to the dropsy. Hydrothorax and edema of the lungs are especially common. Occasionally edema of the larynx supervenes. Extreme distention of the skin sometimes results in dermatitis or even gangrene. Many patients ultimately succumb to secondary infection, which usually takes the form of pneumonia, pleurisy or pericarditis. Intercurrent attacks of acute nephritis may occur at any time. Uremia and albuminuric retinitis sometimes develop at a late period of the disease, but, as already stated neither of these conditions is common.

**Diagnosis.**—Chronic tubular nephritis, even in the early stages cannot readily be overlooked, if the urine is examined at frequent intervals. Without this precaution, however, the disease may readily be confused with *primary neurasthenia* or some *functional disorder* of *the stomach.*

The exclusion of *postural albuminuria* is not always easy, but analyses of the separate urines passed at different times of day, and testing the effect of standing for from twenty to thirty minutes in a pronounced lordotic position will usually lead to a correct diagnosis. The differentiation of an acute exacerbation of a chronic nephritis from an attack of *acute nephritis* has already been considered (see p. 768).

*Chronic glomerulonephritis* can usually be distinguished from chronic tubular nephritis by the abundant urinary secretion, the slight albuminuria, the relatively low and definitely fixed specific gravity of the urine, the excessive blood pressure, the absence or late occurrence of edema, the marked tendency to uremia and to disturbances of vision and the reduced efficiency of the kidneys as shown by functional tests. It must be recognized, however, that mixed forms of the disease are very common and that cases are frequently observed which do not fit accurately in either group.

**Prognosis.**—The prognosis is always grave. Nevertheless, if the disease is of a mild type, as shown by slight urinary changes and complete absence of all active symptoms, life may be prolonged for many years. In such cases, even complete recovery is not impossible, although it is very exceptional. Pronounced and persistent oliguria, copious albuminuria, and extensive and obstinate edema are unfavorable signs. Remissions and exacerbations are common, but the average duration of typical cases is probably 3 or 4 years.

**Treatment.**—The indications are to remove the cause, if possible, to reduce the work of the kidneys by diminishing the production of nitrogenous waste and increasing the activity of the other excretory organs, to maintain the general nutrition, and to meet important symptoms as they arise. Every patient should be carefully examined for foci of infection, and if found, these should be removed. There is ample testimony to show that the eradication of infective foci in the tonsils, teeth, or elsewhere is sometimes followed by an arrest of the disease. The patient must be guarded against vicissitudes of weather by wearing flannel next to the skin in all seasons. If he has adequate means he should be urged to spend the winter months in a warm, equable climate.

In the absence of any obtrusive symptoms, moderate exercise should be encouraged, but excessive muscular effort must be prohibited. Mental strain and worry are also injurious and should be avoided as far as possible. When the symptoms are well developed rest becomes an important factor in in the treatment and much time should be passed in bed. Warm baths with friction are useful in promoting free action of the skin, but great care must be

exercised after their use to prevent chilling. An occasional hot-air or vapor bath at home is often advantageous. Cold bathing should be interdicted. The bowels should be kept active, saline or other cathartics being used for the purpose, if necessary.

A great deal depends upon the diet. No hard-and-fast rules, however, can be laid down, each case being a study in itself. If there are no active symptoms, a simple nourishing diet comprising a moderate quantity of nitrogenous matter, may be allowed, its effects on the blood and urine being carefully observed. Unless there is some indication of nitrogen retention, the proteins should not be reduced below 50 grams per day.[1] Whatever the reduction, the remaining necessary calories must be supplied from carbohydrate and fats. Indeed, considerable caution must be exercised lest in our zeal to relieve the kidneys we reduce the strength of the patient by adhering too strictly to a spare diet. The dogma that red meats are more harmful than white meats is not supported by recent investigations and should be discarded. The various forms of meats are suitable in proportion to their digestibility. Smoked meats and meat extractives should be avoided. Soups, which are unimportant as sources of energy, although usually rich in extractives, should also be excluded from the diet. Condiments, including salt, should be restricted to a minimum. Alcohol is harmful and so also is immoderate smoking.

Unless there is pronounced edema, water-drinking between meals is beneficial, and a mild alkaline mineral water, such as Vichy or Vals, may be taken to the extent of a pint (0.5 L.) or more a day.

No drugs are known that are directly curative. Iron is sometimes useful, but it is indicated only when there is actual anemia, and the indiscriminate use of Basham's mixture or of any other ferruginous preparation is to be deprecated. Myocardial insufficiency requires rest and effective digitalis therapy. A bitter, such as nux vomica or gentian, before meals, may be of service if there is anorexia. Vomiting is best treated by withholding food entirely for a time, and allowing only carbonated water or cracked ice. Such gastric sedatives as bismuth subcarbonate or cerium oxalate, with or without sodium bicarbonate, sometimes afford relief. Sinapisms over the epigastrium may be useful. In persistent vomiting lavage is worthy of trial. If insomnia is sufficiently pronounced to demand the use of a somnifacient, bromids, chloralamid, chloral, or medinal may be tried in the order named. Opium, as a rule, should be avoided.

*Edema.*—Strict limitation of fluids, a rigorous salt-free diet, and rest in bed, or in a chair if the patient is orthopneic, will sometimes cause the dropsy to disappear without other treatment. The Karell diet, although it often meets with serious objections on the part of the patient, is simple and highly effective. It consists in giving 200 mils of milk at intervals of four hours, from 8 o'clock in the morning until 8 o'clock in the evening. No other food or liquid is allowed. If there is much thirst the patient may be permitted to rinse out his mouth with water at intervals, and if hunger is urgent a small piece of dried toast may be given with each portion of milk. If the dropsy is extensive and persistent more active dehydrating measures are required.

Purging with hydragogue cathartics, especially Epsom salt or compound jalap powder, and sweating induced by hot packs or hot-air baths are of value. Pilocarpin, owing to its depressing effects and its tendency to induce profuse bronchial secretion, should, as a rule, be avoided. Diuretics may also be of service. The best are the organic salts of potassium, theobromin,

[1] An average individual on a mixed diet consumes from 75 to 100 grams of protein per day.

caffein, and theocin. When myocardial insufficiency is a factor digitalis is often effective, but not otherwise. The following combination, known as Grainger Stewart's mixture, may be employed:

℞ Potassii acetatis..... ʒii (8.0 gm.)
Infusi scoparii.....
Infusi digitalis.....āā fʒiii (90.0 mils) M.
Sig: A tablespoonful three or four times a day.

Edema that does not yield to the remedies already mentioned may require small incisions on the inner or outer side of each ankle, or the insertion of Southey's tubes. Effusions in the serous cavities sufficient to produce functional disturbances should be removed by paracentesis.

**Surgical Treatment.**—In cases of chronic tubular nephritis that do not respond to the usual measures and are clearly going from bad to worse, decapsulation of the kidneys, as suggested by Edebohls, may be considered. It has not rarely prolonged life and in a few instances it seems to have brought about a complete functional recovery. The good effects of the operation have been ascribed to the relief of tension within the capsule and improvement in the renal circulation.

## CHRONIC GLOMERULONEPHRITIS

**Definition.**—The term chronic glomerulonephritis is applied to a common and dangerous form of chronic renal disease in which the glomeruli bear the brunt of the injury, although the tubules are always more or less affected.

**Etiology.**—The disease may develop out of acute glomerulonephritis, the transition in many instances being interrupted by a longer or shorter period of latency, but sometimes clearly traceable through an intermediate subacute stage.

More frequently chronic glomerulonephritis develops insidiously without an antecedent acute attack, the process being produced gradually by some persistent septic infection, chiefly with streptococci, which have emanated from a primary focus in the tonsils or elsewhere. Doubtless, however, bacteria other than streptococci may sometimes produce the disease. In many cases the etiologic factor is elusive. Occasionally, perhaps, a secondary and hidden localization of infection serves to perpetuate the renal inflammation long after the original focus has disappeared. Whether non-bacterial irritants, such as certain exogenous poisons or noxious substances resulting from deranged metabolism, are capable of slowly attacking the glomeruli is uncertain, but it is not unlikely that such is the case, in as much as the acute form of glomerulonephritis has been produced experimentally by a number of toxic agencies.

Chronic glomerulonephritis is most common in adults between the ages of twenty and forty years, although it is not rare in children, especially after scarlet fever. Males are more frequently affected than females.

**Morbid Anatomy.**—The appearance of the kidney varies with the stage of the disease. At a comparatively *early period* the organ is more or less enlarged, opaque, and of a pale gray color or variegated, reddish areas occurring as a result of hemorrhages or of hemorrhagic pigmentation. The capsule strips readily, revealing a smooth surface. Microscopically, the changes in the early stages are much the same as those in acute glomerulonephritis—occlusion of some of the loops in a certain number of glomeruli by hyaline thrombi, degeneration and proliferation of the glomerular epithelia, albuminous exudations into the capsular spaces, fatty degeneration and detachment of the tubular epithelium, and infiltration of the interstitial

tissue with wandering cells—although evidences of chronicity, such as sclerotic thickening of the glomerular capsules, proliferation of connective tissue between the glomeruli and tubules and atrophy of some of the tubules, are not wanting.

In *advanced cases* (secondarily contracted kidney) the kidney is small, firm and of a reddish-gray or reddish-yellow color. The capsule is thickened and adherent, and when removed reveals a smooth or, more frequently, a granular surface, with a variable number of small cysts. The cortex is narrowed and its markings are indistinct. Microscopically, the glomeruli in many places are atrophied or completely transformed into small fibrous or hyaline globules surrounded by concentric layers of fibrous tissue. Usually, however, a sufficient number of glomeruli with acute or subacute lesions still remain to show that these were the histologic elements primarily affected. Many of the tubules are shrunken or obliterated, others are distended, and some still contain casts. The interstitial tissue between the glomeruli and tubules is everywhere increased and is in all stages of development from the fibroblastic to the cicatricial. The blood vessels of the kidney almost invariably show sclerotic changes—thickening of the intima and narrowing of the lumen.

**Symptoms.**—In some cases the disease develops directly out of acute glomerulonephritis, the symptoms of the latter never entirely disappearing. As the condition passes from the acute to the chronic form the anemia usually becomes more pronounced, the blood pressure rises, sometimes reaching 180 and even 200 or more, and the urine, which was at first scanty, gradually becomes thin (hyposthenuria) and more plentiful, although it continues to show a considerable quantity of albumin, with casts of various kinds and erythrocytes. If edema was present at first, it may persist, otherwise it may be wanting throughout. After the lapse of months, headache, nausea and vomiting often appear, and there may be uremic convulsions or coma.

In the majority of cases, however, chronic glomerulonephritis develops insidiously and is discovered accidentally or escapes recognition until the last stages, when the more severe symptoms begin to appear. Failure of general health, loss of flesh and strength and increasing anemia may be the first obtrusive manifestations. The tendency to anemia is usually proaounced, and eventually the patient often acquires a peculiar cachectic nppearance not unlike that occurring with malignant disease. Symptoms referable to the gastrointestinal tract, such as anorexia, fetor of breath, nausea and attacks of vomiting or diarrhea, are very common, and are likely to be ascribed, at least for a time, to some other cause than nephritis. In other cases the disease is made manifest by headache, muscular pains, vertigo, and tinnitus aurium, these symptoms being due to increased arterial tension or to chronic uremia. In still other cases dyspnea, palpitation, and a sense of oppression about the heart are prominent features. Suffocative attacks resembling asthma are not uncommon. These occur especially at night and are usually to be attributed to circulatory embarrassment and acute pulmonary edema (see p. 605), although occasionally they seem to be of uremic origin. Sometimes the respiratory disturbance takes the form of Cheyne-Stokes breathing, a phenomenon, which is always of serious import.

The blood pressure is almost invariably increased, a systolic figure of 200 to 250 and a diastolic figure of 120 to 160 being not unusual. Even at a comparatively early period, physical examination usually reveals some hypertrophy of the heart, especially of the left ventricle, with a loud and prolonged first sound in the mitral area and an accentuated, ringing second

sound in the aortic area. Eventually, dilatation of the heart often occurs secondarily to the hypertrophy, and in this event, a soft systolic murmur appears in the mitral area and the second sound loses its ringing character. In long-standing cases thickening and tortuosity of the peripheral vessels and other signs of general arteriosclerosis are also commonly present.

Owing to the high blood pressure and retrograde changes in the vessels, hemorrhages may occur from the nose, from the kidney itself, or into the brain, skin, or other structures. The brain is one of the favorite sites, hence chronic nephritis must be regarded as an important cause of cerebral apoplexy.

*Edema* of renal origin is exceptional unless the glomerular lesions are associated with extensive degeneration of the tubular epithelium (diffuse nephritis). It is observed chiefly in the cases that develop rapidly out of the acute form of glomerulonephritis. In the end-stage swelling of the feet and legs and even generalized dropsy may occur, however, as a result of cardiac failure. Occasionally edema of the larynx or hydrothorax develops abruptly without generalized dropsy.

*Retinal changes* occur more frequently in chronic glomerulonephritis than in other form of renal disease and are of considerable diagnostic value. Usually both eyes are affected. Typical cases are characterized by the appearance in the neighborhood of the macula of opaque, white patches, variously shaped, but often stellate. Especially significant is the presence of a ring-shaped zone of white exudation around the nerve-head—the so-called "snow-bank" appearance. A less characteristic feature is occurrence of hemorrhages, frequently linear or flame-shaped, but sometimes large and diffuse. In other cases still, the optic papilla is intensely congested or the nerve-head is so swollen as to form a picture indistinguishable from that of optic neuritis (choked disc), the result of increased intracranial pressure.

Impairment of vision usually results from these ocular lesions and may first attract attention to the underlying disease. Sometimes, however, the sight is so little affected that the retinal changes would remain unrevealed unless especially sought for by an ophthalmoscopic examination. Occasionally, amblyopia or amaurosis occurs as a manifestation of uremia, in which case the ophthalmoscope may show no striking abnormalities. Accompanying the retinitis, or occurring independently of it, if the blood pressure is very high, there is sometimes a pronounced staring expression of the eyes or even a considerable degree of exophthalmos.

*Uremia* of the convulsive or comatose type supervenes sooner or later in a large proportion of cases. As a rule its occurrence is presaged by various nervous or digestive disturbances, but occasionally it develops without warning, while the patient is still in apparently good health.

Persistent *dyspnea* is rarely absent in the terminal stages of the disease. It may be due to cardiac insufficiency, hydrothorax, pulmonary edema, uremia or acidosis, or to any combination of these factors.

The *urine* is pale in color and abundant (2000 to 4000 c.c.), the quantity of the night urine in particular being frequently excessive. Indeed, true nocturia, or the voiding of more than 450 c.c. at night when no excess of fluid is taken (see p. 764), is one of the earliest indications of the disease. Accompanying the polyuria, there is usually increased frequency of micturition, especially at night (nocturnal pollakiuria), but this phenomenon without reference to the total quantity of urine is less significant. Even upon the approach of uremia the volume of urine often remains large. The percentage and eventually the total amount of urea and other nitrogen waste products

are less than normal; the specific gravity of the urine is low and somewhat definitely fixed at from 1010 to 1013. The amount of albumin in the urine is usually small, often not more than a trace, and at times none may be present. Sometimes only the late afternoon urine or that voided after exercise is albuminous. The sediment is scanty. It contains a variable number of hyaline and pale granular casts. Leucocytes and erythrocytes may also be present.

In the later stages of the disease the functional capacity of the kidneys is always more or less impaired, as shown by the low nitrogen and sodium chlorid content of the urine collected in two-hour portions with the patient on a special diet, the low phenolsulphonephthalein output within two hours, and the high urea and creatinin content of the blood, etc. (see p. 765).

**Complications.**—Reference has already been made to retinitis, cerebral and other hemorrhages, dilatation of the heart, pulmonary edema, and uremia. Owing to the impaired resistance of the tissues, secondary infections of various kinds are common; the most important are pneumonia, bronchitis, pleurisy and pericarditis. Certain affections of the skin, such as eczema, urticaria and generalized pruritus, occasionally occur, and even widespread erythematous or bullous eruptions have been observed.

**Diagnosis.**—A disease that appears under so many different guises as chronic glomerulonephritis must necessarily fail of recognition in many cases unless the urine and circulatory condition of every patient are systematically examined. High blood pressure itself should always arouse suspicion, although it may be due, of course, to other causes than nephritis. If it is accompanied by nocturnal polyuria and a definite fixation of the specific gravity of the urine at 1010–1013 (hyposthenuria) the presence of chronic nephritis may be assumed, even in the absence of albuminuria and cylindruria.

The differential diagnosis between chronic glomerulonephritis with secondary dilatation of the heart and *primary cardiac insufficiency with secondary congestion of the kidneys* may be difficult without reference to the past history of the patient and the application of the therapeutic test. However, a low water output, with high specific gravity and a normal nitrogen excretion after a nephritic test meal (see p. 764) is opposed to serious structural changes in the kidneys. In simple renal congestion, too, the waste nitrogen in the blood is not usually much increased, and while the phenolsulphonephthalein excretion is often greatly impaired, it is, as a rule, rapidly reëstablished with the restoration of cardiac compensation. The distinction between chronic glomerulonephritis and *chronic tubular nephritis* is not always easily drawn, because of the very frequent occurrence of mixed forms (diffuse nephritis) in which the symptoms are equivocal, but the following table will indicate the principal points of difference:

| Chronic Tubular Nephritis | Chronic Glomerulonephritis |
|---|---|
| Edema usually appears early and is often pronounced. | Edema is usually absent or confined to the end stage, when the circulation fails. |
| The blood pressure is usually normal or nearly normal. | The blood pressure is high. |
| Uremia is uncommon. | Uremia is common. |
| Albuminuric retinitis is exceptional. | Albuminuric retinitis is common. |
| The urine is diminished in quantity. | The urine is increased in quantity, especially at night. |
| The specific gravity of the urine is variable, but usually at a high level. | The specific gravity of the urine is fixed and at a low level. |
| Albuminuria is marked. | Albuminuria is slight and at times may be absent. |
| Tube-casts are numerous. | Tube-casts are few in number. |
| Functional capacity of the kidney is often about normal. | Functional capacity of the kidneys is usually impaired. |

*Diabetes insipidus* resembles chronic glomerulonephritis in causing an excessive excretion of pale, watery urine, but it is not attended with high blood pressure, albuminuria, cylindruria, or any incapacity on the part of the kidneys to excrete phenolsulphonephthalein or other dyes. Chronic nephritis may cause virtually all of the symptoms of *brain tumor*, including choked disc, but the blood pressure reading and the findings of the urinalysis will usually prevent an error in diagnosis.

**Prognosis.**—The prognosis of fully developed chronic glomerulonephritis, so far as recovery is concerned, is altogether unfavorable. In mild cases, however, the patient's condition may remain comparatively good for a number of years, and in the initial stage, before any signs of cardiac or arterial disease are present, partial or even complete recovery is possible if the underlying cause can be found and removed. The entire duration of the disease cannot, as a rule, be positively determined because of the insidious onset, but, on the whole, it is decidedly shorter than that of chronic tubular nephritis and more steadily progressive. Pronounced cardiovascular signs, retinal lesions, a low 'phthalein excretion (less than 30 per cent. in two hours), unless it is due to some extrarenal factor, such as myocardial insufficiency, and, especially, any considerable increase in blood urea or total incoagulable nitrogen are unfavorable features. The majority of patients die within two years after the development of albuminuric retinitis, although some survive for a much longer period. The number and character of the casts and the amount of albumin in the urine are of little value as guides to prognosis. Not rarely in severe cases bordering on uremia the urine is free from casts and shows little or no albumin. Functional tests are exceedingly helpful in measuring the efficiency of the kidneys, and, when applied repeatedly, in determining whether nephritis is stationary or progressive and the rate of progress, but alone they are inadequate from the viewpoint of prognosis, for death frequently occurs from cerebral hemorrhage, cardiac insufficiency, angina pectoris, an acute exacerbation superimposed upon the chronic process or some other factor concerning which they can give no information.

**Treatment.**—The treatment in general is similar to that of chronic tubular nephritis (see p. 773). The important features are the removal of any focus of infection in the tonsils, about the teeth, in the prostate, or elsewhere or of any toxic condition that may be responsible for the nephritis, regulation of the diet, especially as regards proteins, and the avoidance of mental and physical strain, overeating, immoderate use of tobacco, chilling of the body and all other factors that may increase the blood pressure or bring about insufficiency of the myocardium.

As regards the diet, if the 'phthalein output is normal and there is no increase in the blood nitrogen, the protein intake should not be reduced below 50 or 60 grams,[1] as this amount is necessary in maintaining the nutrition of the body. To make up the required number of calories (2000) the amount of carbohydrate and fat food should be correspondingly increased. Except in the matter of digestibility, it makes little difference in what form

[1] 28.3 gm. (1 oz.) of cooked *beef* yields about 6–8 gm. of protein.
28.3 gm. (1 oz.) of cooked *lamb* yields about 6 gm. of protein.
28.3 gm. (1 oz.) of cooked *chicken* yields about 6–8 gm. of protein.
28.3 gm. (1 oz.) of cooked *fish* yields about 6 gm. of protein.
28.3 gm. (1 oz.) of cooked *beans* yields about 1–2 gm. of protein.
28.3 gm. (1 oz.) of cooked *potatoes* yields about 0.6 gm. of protein.
28.3 gm. (1 oz.) of cooked *green vegetables* yields about 0.5 gm. of protein.
28.3 gm. (1 oz.) of cooked *wheat bread* yeilds about 2.0 gm. of protein.
28.3 gm. (1 oz.) of cooked *tapioca pudding* yields about 3.0 gm. of protein.
1 *egg* yields about 6–7 gm. of protein.

of food, whether beef, mutton, chicken, fish, eggs, or beans, the protein is supplied. In marked renal insufficiency with low 'phthalein output and cumulative phenomena, the protein-bearing foods should be restricted to a minimum or for short periods withheld altogether. Moderation in the use of liquids is important, for the consumption of an excessive amount of fluid puts an extra burden not only upon the kidneys, but also upon the heart and bloodvessels. This is one of the objections to an exclusive milk diet. Unless the disease is far advanced it is often desirable for the patient to spend the winter months in a warm, dry, equable climate. Altitudes above 1000 feet, however, should be avoided if the cardiovascular changes are at all marked.

In the treatment of the disease in its early stages drugs play but a minor role. Iron has been extensively used, but it is contraindicated unless there is actual anemia, and even then only moderate doses should be prescribed and its effects should be carefully observed. The high blood pressure is a compensatory factor enabling the kidneys to maintain adequate function. If the arterial tension is excessive it may be brought within bounds by rest, restriction of the diet, free purgation, and, if necessary, the abstraction of a few ounces of blood. Vasodilators, such as nitroglycerin and sodium nitrite, should, as a rule, be reserved for emergency and used only for short periods. If used too freely they may precipitate uremia. The occurrence of myocardial insufficiency, as shown by dyspnea on exertion, slight edema of the legs, a decrease in the daily excretion of urine, etc. is, to be combated by rest, the use of foods of small bulk, and the administration of digitalis in doses sufficient to produce a perceptible effect on the heart. The digitalis is indicated irrespective of the degree of arterial hypertension. Theobromin or caffein is also of service in some cases. Severe renal insufficiency, with dyspnea, restlessness and insomnia, requires rest in bed or, if necessary, in a chair, and usually the use at night of some general sedative, especially chloral, 5 to 10 gr. (0.3–0.6 gm.) opium, 1 gr. (0.06 gm.) in suppository, or morphin, $\frac{1}{8}$–$\frac{1}{4}$ gr. (0.008–0.016 gm.) hypodermically. Occasionally, moderate doses of a bromid, alone or in combination with a nitrite, suffice. Impending uremia may sometimes be averted by complete rest, restriction of the diet to milk, free purgation, hot packs, and the use of a diuretic of the caffein group (caffein, theobromin or theocin). Digitalis may prove invaluable if myocardial insufficiency is a factor. The treatment of actual uremia has already been considered (see p. 770).

## ARTERIOSCLEROTIC CONTRACTED KIDNEY

### (Primary Contracted Kidney)

**Definition.**—The term arteriosclerotic contracted kidney is applied to a form of chronic renal disease in which more or less of the parenchymatous substance of the kidney suffers atrophic loss and is replaced by scar tissue as a result of a primary sclerosis of the bloodvessels and a gradual diminution of the blood supply of the organ. The condition originates in a widespread disease of the arteries, in which the smaller arterioles especially are affected (arteriocapillary fibrosis of Gull and Sutton), and is to be distinguished from primary sclerosis of the kidney following acute interstitial non-suppurative nephritis (see p. 759), from secondary renal sclerosis following glomerulonephritis (secondary contracted kidneys), and even from the atrophic kidney of senile arteriosclerosis.

**Etiology.**—Arteriosclerotic contracted kidney is merely part of general arteriosclerosis and therefore the causes of the one condition are the causes

of the other. The disease usually begins in the fourth or fifth decade of life and males are somewhat more subject to it than females.

**Morbid Anatomy.**—The macroscopic appearance of the kidney does not differ from that of renal sclerosis resulting from protracted glomerulonephritis. The organ is small, hard, and usually dark red in color, but sometimes pale. The capsule is thickened and usually adherent, and when stripped off reveals a granular or nodular surface, which is often studded with a variable number of small cysts. On section, the kidney is abnormally dense, the arteries are thick-walled and rigid, the cortex is considerably narrowed, and the pelvis is relatively large or even actually dilated and often contains an increased amount of fatty tissue.

Microscopically, the conspicuous features are a great increase of fibrous connective tissue, sclerosis of the arterioles with marked intimal thickening, and degenerative atrophy of the tubules and glomeruli. The fibrosis, which is mainly of cicatricial character, is especially pronounced about the glomerular capsules and the small arteries. All the arteries show intimal thickening with narrowing of the lumen. Wherever the connective tissue is most abundant and dense the tubules are compressed or completely occluded and lie very close together. In some of the tubules the epithelium is much lower than normal, in others it is atrophic and desquamated, and in others still it is lost. Here and there, probably as a result of localized obstruction, segments of tubules are dilated into cysts. In the cicatricial areas the Malpighian bodies also are more closely packed, as a result of gradual occlusion of the vessels and direct compression, and present varying degrees of degenerative atrophy. The capsule is greatly thickened, owing to a deposit of hyaline material or to new connective tissue formation and the glomerulus itself is collapsed and shrunken. In advanced cases many of the Malpighian bodies are transformed into small fibrous masses or hyaline globules, surrounded by concentrically arranged connective tissue. In the uncontracted areas, which correspond to the gross irregularities on the surface of the kidney, the Malpighian bodies, as well as the uriniferous tubules, may be normal or, as a result of compensatory hypertrophy, very much enlarged. At no stage of the process in pure arteriolar renal sclerosis do the Malpighian bodies show the distinctively inflammatory changes—thrombotic occlusion of the capillaries, proliferation of the glomerular epithelia, albuminous exudation in the glomerular spaces, adhesions between the glomerulus and the capsule, etc.—that are characteristic of glomerulonephritis, although in both conditions the end result is the same, and with the occurrence of extensive tissue destruction, scarring and distortion it is quite impossible to decide whether the changes have originated in the glomeruli or, in the bloodvessels. It must be borne in mind, also, that in some cases true inflammatory changes in the glomeruli and ordinary arteriosclerotic changes in the bloodvessels coexist in the same kidney—the combination form of Volhard and Fahr.

In addition to the lesions in the kidneys, the bodies of persons dying of arteriosclerotic contracted kidney also show widespread arteriosclerosis and hypertrophy of the heart, usually with secondary dilatation and especially marked in the left ventricle.

**Symptoms.**—The symptoms are largely those of hypertensive cardiovascular disease (see page 730) and of general arteriosclerosis, the renal condition being more or less incidental. Many cases are latent for years and fail of recognition until discovered accidentally in a routine examination for life insurance or until the occurrence of a serious or fatal complication. Some patients complain of undue tendency to fatigue, palpitation on exertion, headache, neuralgias or myalgias in various regions, and vertigo. For a long

period, however, there may be no change in their color or general nutrition. With the occurrence of myocardial insufficiency and dilatation of the heart, dyspnea, asthmatic attacks at night, precordial discomfort, edema, effusions in the serous sacs, gastrointestinal disturbances, etc., make their appearance. Hemorrhages from the mucous membranes, especially that of the nose, and into the conjunctiva, retina, and cerebrum are common. Attacks of bronchitis and of pulmonary congestion are also somewhat frequent. Uremia is relatively rare, although it may occur late in the disease when the heart fails. While retinal hemorrhages are common, true albuminuric retinitis is seldom observed.

The chief cardiovascular signs are increased blood pressure, thickening and rigidity of the walls of the accessible arteries, accentuation of the aortic second sound, and enlargement of the heart, especially of the left ventricle. With cardiac dilatation a systolic murmur usually develops at the apex, probably as a result of relative mitral insufficiency. The blood pressure may reach excessive heights, readings of 200 to 250 being not infrequent.

The urine may be normal in amount, but there is a tendency toward polyuria, and frequently the patient has to get up two or three times at night to empty the bladder. The specific gravity of the urine is, as a rule, low, although it is not so definitely fixed as in glomerulonephritis. Traces of albumin and a few hyaline and granular casts are usually present. With the occurrence of cardiac failure the urine may become scanty and the albuminuria pronounced. Functional tests reveal little or no reduction in the efficiency of the kidneys until the disease is far advanced.

**Diagnosis.**—The diagnosis is not usually difficult, especially if the course of events is known. *Chronic glomerulonephritis with secondary cardiovascular changes*, as distinguished from primary arteriosclerotic contracted kidney, is characterized by more serious disturbance of the general health, pronounced polyuria with fixation of the specific gravity of the urine at a low level, decreased efficiency of the kidneys as shown by functional tests, and a marked tendency to albuminuric retinitis and to uremia. When glomerulonephritis and primary arteriolar nephritis coexist the clinical features of the former dominate the clinical picture.

**Prognosis.**—The prognosis is that of the underlying vascular disease. A duration of 5, 10 or even 15 years is not uncommon. When death occurs it is rarely the result of uremia, but is usually due to cardiac insufficiency to an arterial accident, such as cerebral hemorrhage, to angina pectoris, or to some intercurrent infection, especially pneumonia.

**Treatment.**—The treatment is that of the primary cardiovascular disease, modified sometimes in the final stages by conditions that have been produced by the secondary nephritis.

## PYELONEPHRITIS

**(Pyelitis)**

**Definition.**—The term pyelonephritis is applied to septic infection involving both the pelvis of the kidney and the renal parenchyma, In many cases the ureters and bladder are also affected. Pure pyelitis is uncommon, as an infection attacking the pelvis of the kidney first almost invariably extends to the renal parenchyma, and an infection beginning in the latter usually spreads to the renal pelvis. Not rarely, however, the infection of the parenchyma is slight and soon subsides leaving the pelvis alone involved. The disease may

be unilateral, although, as a rule septic infection in one kidney sooner or later causes inflammation in the other.

**Etiology.**—The microörganisms most frequently concerned in the process are colon bacilli, staphylococci, streptococci, and tubercle bacilli. Mixed infections are not uncommon. The disease may follow one of the general infections, such as typhoid fever, influenza, septicemia or scarlet fever, or it may have its source in the intestinal tract (enteritis, appendicitis, intestinal stasis, etc.) in the bladder (cystitis) or one of the other pelvic organs, or in some more distant focus, such as the tonsils, a boil, an infected tooth, etc.

Certain predisposing factors are operative in a very large proportion of cases. Foremost among these are (1) obstruction of the urinary passages by enlarged prostate, urethral stricture, pelvic tumor, pregnant uterus or kinking of the ureter, as in floating kidney; (2) the presence of a calculus, a tumor, or tubercle in the renal pelvis; (3) excretion of irritating drugs, such as oil of turpentine, copaiba, cantharides, etc.; (4) chilling of the body; and (5) traumatism. Clinically, four groups of cases are especially important: those occurring in young children, those developing in pregnant women, those associated with renal calculi, and those dependent upon cystitis.

Pyelonephritis in children is much more common than was formerly supposed. It is usually due to the colon bacillus and about three-fourths of the cases are observed in girls. It is twice as frequent in children under two years as it is after that age (Thomson[1]). The disease may accompany or follow one of the specific fevers or it may depend upon chilling of the body, but in the majority of cases it is associated with some intestinal disturbance, chiefly diarrhea. The pyelonephritis of pregnancy usually develops during the second half of gestation and in three-fourths of the cases it is excited by the colon bacillus. Compression of the ureters by the gravid uterus is thought to be an important predisposing factor. Nephrolithiasis is apparently not due to renal infection but to over-saturation of the urine with crystalloids or to changes in the composition of the urine which decrease its solvent power. Once a calculus has been formed, however, it may cause pyelitis or aggravate the inflammatory process if one already exists. Cystitis is especially prone to cause pyelonephritis when it is accompanied by obstruction of the ureters or urethra. The infection may be due to colon bacilli alone, but more frequently it is produced by a mixture of colon bacilli and pyogenic cocci.

The route by which the infection enters the kidney from the various portals of entry has been the subject of considerable discussion. Recent studies, however, have tended to establish the blood as the usual means of transport. Even the renal infections originating in the intestine or lower urinary passages seem to be, as a rule, hematogenous, although the possibility of the transference of bacteria from the colon or bladder to the kidney by the lymphatics or from the bladder directly through the ureter cannot be denied. The essentials for ascending or intraureteral infection appear to be insufficiency of the ureterovesical valve and impairment of the ureteral peristalsis.

**Morbid Anatomy.**—The changes in the kidney in pyelonephritis vary with the type of organism that has produced them. In the cases caused by colon bacilli alone the pelvis of the kidney is for a long time the part chiefly affected, although at the onset microscopic examination of the renal tissue may show cloudy swelling of the epithelium of the convoluted tubules and slight cellular infiltration of the intertubular connective tissue. During the acute stage the mucous membrane of the pelvis is congested, swollen and covered with mucopus. In the more chronic cases the mucous membrane becomes thickened, discolored and sometimes more or less eroded. The

[1] Brit. Med. Jour., Aug. 23, 1913, 482.

mucous membrane of the ureter and bladder frequently shows similar changes, and eventually the kidney substance may become secondarily invaded from the pelvis. When there is any impediment to the escape of pus, the pelvis and calices become distended and the renal parenchyma undergoes atrophy from pressure, the kidney being gradually transformed into a cyst filled with purulent fluid (*pyonephrosis*).

In the second, smaller, but more serious group of cases, in which the invading organisms are pyogenic cocci—Staphylococcus pyogenes albus and aureus and Streptococcus pyogenes—the renal parenchyma is extensively involved. The kidney is congested and its substance, especially the cortex just beneath the capsule, often presents numerous miliary abscesses, some of which extend as opaque yellow streaks downward toward the pyramids. If the process continues these abscesses may increase in size and coalesce, thus forming large pockets of pus, which may eventually break through the renal capsule and produce perinephritic abscess. The mucosa of the pelvis may also be intensely inflamed, but not rarely it escapes and the urine remains clear, at least for a time, as compression of the collecting tubules by the swollen tissue surrounding them prevents the pus from reaching the orifices in the papillæ (Cunningham,[1] Cabot and Crabtree,[2] Judd[3]).

**Symptoms.**—In its acute form the disease usually begins suddenly with chilliness or a chill, fever and pain in the loins and lower abdomen, sometimes severe and marked by exacerbations suggesting renal colic. Nausea and vomiting may also occur. Frequently in young children infection of the kidney is preceded or accompanied by diarrhea. The temperature may be as high as 104° or even 105° F., and the fever may be of the continuous type with moderate remissions, as in typhoid fever, or it may be irregular with pronounced fluctuations, as in septicemia. Occasionally the fever is intermittent, the temperature rising only when the free escape of pus is interrupted. Leucocytosis is the rule, and may be marked. Physical examination often reveals tenderness and muscular rigidity in one or both flanks or over one or both kidneys anteriorly. Anorexia and restlessness are almost constantly present and as the disease progresses the patient loses weight and becomes anemic. In infants the pallor may be intense. In fulminating cases, or those with multiple abscesses in the kidney, toxemia rapidly develops, delirium sets in, and death occurs within a few days, unless the disease is unilateral, which is not rarely the case, and the offending organ is removed. On the other hand, there are many mild cases of colon-bacillus infection in which pain and tenderness are slight or absent and the chief constitutional disturbance is recurring pyrexia, especially toward evening, over a period of several weeks. Even when the infection is severe uremic symptoms are uncommon, but they may develop if the renal tissue is extensively damaged.

Urinary symptoms may be wanting, but not rarely micturition is frequent and painful. The urine is usually turbid, and in colon bacillus infection it is almost invariably acid. The degree of pyuria varies in different cases and from time to time in the same case. Frequently, pus is revealed only by microscopic examination of the urinary sediment. In many cases, however, it is present in large amount. Not rarely pus is temporarily absent owing to blocking of the ureter on the affected side; hence the importance of examining several specimens of urine in all doubtful cases. There is no close relation between the degree of pyuria and the gravity of the condition; indeed, in some of the most severe infections due to pyogenic cocci the urine

[1] Jour. Amer. Med. Assoc., 1915, lxiv, 230.
[2] Surg., Gynec. and Obst., 1916, xxiii, 495.
[3] Ann. of Surg., 1917, lxvi, 362.

contains only minute quantities of pus. Even when the pus is scanty bacteria are usually present in considerable numbers. After filtering out the pus a small amount of albumin may or may not be present. Tube-casts are, as a rule, absent unless the infection is due to cocci and involves the renal substance (Rovsing). According to Cabot and Crabtree,[1] if the freshly drawn urine shows cocci in abundance, with a small amount of albumin, a few red blood cells and many leucocytes or a little pus, with normal or nearly normal 'phthalein excretion, the diagnosis of coccus infection is justified; on the other hand, if examination of the urine shows many bacilli, a little albumin, and much pus, with marked diminution of 'phthalein excretion, a diagnosis of colon bacillus infection is unavoidable.

*Chronic pyelonephritis* may go on for years with little evidence of its presence other than pyuria. This is particularly true when the infection is due to the colon bacillus. Recurring attacks of fever and pain, however, are common and are usually due to acute exacerbations or to obstruction of the ureter of the affected kidney and retention of pus. More or less enlargement of the diseased kidney is often observed on palpation (pyonephrosis). When the disease is bilateral and much of the renal tissue is involved, anemia, high blood pressure and enlargement of the heart may supervene, and eventually the patient may die of uremia. The urine is frequently increased in amount owing to secondary arteriolar or glomerulonephritis. Its reaction may remain acid, but in many cases, especially when the disease is secondary to cystitis, it becomes alkaline from ammoniacal decomposition. Occasionally, attacks of hematuria are brought on by the extension of ulcers in the pelvis of the kidney.

**Diagnosis.**—The diagnosis is usually not difficult, but many cases are overlooked because frequently the symptoms do not point definitely to the kidneys. In all obscure febrile conditions without localizing symptoms, repeated examinations of the urine should never be omitted. Acute cases with abdominal pain and tenderness may readily be mistaken for *ileocolitis*, *appendicitis*, or *cholecystitis*. It must be borne in mind that in infancy the association of pyelonephritis with ileocolitis is common, and that in older children and adults infection of the right kidney and appendicitis may also coexist.

The question whether a case is one of uncomplicated cystitis or of cystopyelonephritis cannot always be answered satisfactorily without recourse to cystoscopy and ureteral catheterization. The presence of dysuria and increased frequency of micturition does not, of course, justify the exclusion of pyelonephritis, but the absence of these symptoms is opposed to cystitis. The shape of the epithelial cells in the urinary sediment is without diagnostic significance.

The distinction between acute pyelonephritis and the *ordinary forms* of *nephritis* is not difficult. In the latter the urine contains a much larger percentage of albumin, the urinary sediment shows many tube-casts but few pus cells and bacteria, the efficiency of the kidneys as shown by functional tests is always reduced, and edema is frequently present.

*Renal calculus* can be excluded definitely only by x-ray examinations or the use of the wax-tipped ureteral catheter. The differential diagnosis between simple pyelonephritis and *tuberculosis of the kidneys* may be made by careful consideration of the past history, by thorough physical examination, by the use of the cystoscope, which often shows suggestive changes in the trigon or ureteral meatus, by bacteriologic studies of urine which has been obtained by catheter so as to avoid contamination with the smegma bacillus, and by application of the tuberculin tests.



[1] Surg., Gynec, and Obst., 1916, xxiii, 495.

After the diagnosis of pyelonephritis has been made, cystoscopy and ureteral catheterization are invaluable in determining whether the disease is unilateral or bilateral and if unilateral, which organ is affected, and functional tests are indispensable in determining to what extent the renal tissue itself has been damaged.

**Prognosis.**—The prognosis depends upon the nature and severity of the infection and whether or not the cause is one that can be readily removed. In acute cases due to the colon bacillus the prognosis, is as a rule, good, although the disease shows a decided tendency to relapse and to become chronic. In children under two years of age the mortality is 10–15 per cent. The pyelonephritis of pregnancy, if recognized early and properly treated, usually terminates favorably. Severe cases of pyelonephritis due to pyogenic micrococci often end fatally, unless the disease is unilateral and the affected kidney is promptly removed or decapsulated and drained. Chronic pyelonephritis, even under favorable conditions, is intractable to treatment, although it often persists for years without seriously impairing the patient's general health. In no case of pyelonephritis should cure be regarded as complete until the urine is sterile for a long period, as well as free from pus.

**Treatment.**—In acute cases medical treatment consists of locating and removing, if possible, the underlying cause, in keeping the patient at rest in bed, in restricting the diet to bland, easily digestible food, in giving an abundance of water, in securing free evacuation of the bowels, in administering urinary antiseptics or, in colon bacillus infections, sufficient alkali to render the urine definitely alkaline, and, if the infection is a stubborn one, in using autogenous vaccines.

Hexamethylenamin is the best urinary antiseptic. It may be given in doses of 5 to 10 gr. (0.3–0.6 gm.) four times a day. The efficiency of the drug depends upon the liberation of formaldehyde and this occurs only in acid urine; therefore, if the urine is alkaline it should first be made acid by the administration of acid sodium phosphate. It must be borne in mind, also, that in large doses hexamethylenamin is capable of producing hematuria. Salol is sometimes useful. It may be given alone or in combination with hexamethylenamin. In many cases of pyelonephritis due to the colon bacillus alkalies give better results than urinary antiseptics. Potassium citrate or potassium bicarbonate, or a mixture of the two, may be selected and given to adults in doses of 20 to 30 grains (1.3–2.0 gm.), four times a day, or to infants in doses of 10–15 grains (0.6–1.0 gm.) four times a day. The exact amount may be determined by testing the reaction of the urine. Not rarely success is achieved by alternating courses of hexamethylenamin and alkalies, administering each for a period of a week. In obstinate cases autogenous vaccines should be given a trial. While they often fail, they sometimes produce marked improvement, especially in colon bacillus infections. The injections should be given every few days and the dose gradually increased from 10 million organisms to 500 million or more. In some cases after failure of internal remedies a cure has been effected by lavage of the renal pelvis with silver nitrate solution (1 : 10,000).

In pyelonephritis gravidarum it is sometimes, but not often necessary to bring the pregnancy to an end. In pyelonephritis due to pyogenic cocci surgical intervention is often required, but it should be deferred, unless the toxemia is profound, until medical measures have had a thorough trial.

The treatment of *chronic pyelitis* resulting from renal calculus, stricture or kinking of the ureter, prostatic enlargement, etc. is largely that of the primary condition.

# NEPHROLITHIASIS

(Renal Calculus; Stone in the Kidney)

**Varieties.**—Concretions may be formed in the uriniferous tubules or in the pelvis of the kidney. Those formed in the tubules are often incorrectly spoken of as *infarcts*. The latter include the deposits of urates frequently found in newborn infants and in gouty subjects, of calcium salts sometimes seen in the aged and in persons poisoned with corrosive sublimate and other substances, and of pigment found in jaundice and hemoglobinuria. These so-called infarcts rarely produce any disturbance, although the uric-acid deposits occasionally give rise to hematuria.

Concretions occurring in the pelvis of the kidney are known as *renal calculi*. In size they vary from minute particles of grit to masses an inch or more in diameter. MacGregor[1] has described a stone weighing 55 ounces (1710 grams), and Gee[2] one weighing 36 ounces (1120 grams). They may be solitary or multiple. When numerous they are usually very small. Bland-Sutton[3] found more than 40,000 discrete calculi in one kidney. Minute concretions are often referred to as *renal sand* or *gravel*. In from 10 to 15 per cent. of the cases of nephrolithiasis both kidneys are involved. Many calculi show a distinct nucleus surrounded by lamellæ, which may not all be of the same composition.

The chief constituents of renal calculi are (1) uric acid, (2) calcium oxalate and (3) ammonio-magnesium and calcium phosphate. In rare instances calculi are formed of calcium carbonate, cystin, xanthin, or saponaceous matter probably derived from degenerated epithelium (urostealith calculi).

*Uric-acid calculi* are yellowish or reddish-brown in color, hard, brittle, smooth or slightly granular, and when multiple, often faceted. *Calcium oxalate* calculi are dark in color, heavier and much harder than uric-acid calculi, and usually rough or actually spinous.

*Phosphate calculi* are grayish in color, friable, and lighter in weight than either uric-acid or oxalate stones.

In the large majority of cases more than one urinary constituent is present, and not rarely uric acid, calcium oxalate and phosphates are all contained in the same calculus. In this country the most common urinary concretion is one consisting of variable proportions of uric acid and calcium oxalate. Phosphatic concretions are known as secondary calculi because they are produced by ammoniacal decomposition of the urine, the result of bacterial invasion. Pure forms are rare in the kidney, although uric acid and other calculi are often heavily incrusted with phosphates. Renal sand is usually formed of uric acid.

**Etiology and Pathogenesis.**—Nephrolithiasis occurs at all periods of life, but it is most common between the ages of 15 and 45 years In 9 of 157 cases analyzed by Hugh Cabot[4] and in 6 of 201 cases analyzed by Keyes[5] the onset of symptoms was in the first decade. The disease is much more frequent in males than in females. Its prevalence varies in different localities; thus, the natives of lower China and upper India are especially susceptible, while the negro races of Africa are comparatively immune (Pfister[6]).

The mode of formation of renal calculi still remains undetermined. Whatever the fundamental etiologic factors, however, the immediate cause of nephro-

[1] Amer. Jour. Med. Sci., Jan., 1877.
[2] Trans. Roy. Med. and Chirurg. Soc., lvii, 1881.
[3] Brit. Med. Jour., Jan. 21, 1905.
[4] Jour. Amer. Med. Assoc., Oct. 9, 1915.
[5] Amer. Jour. Med. Sci., Mar., 1921.
[6] Arch. f. Schiffs-u. Tropenhygiene, 1913, p. 599.

lithiasis is an oversaturation of the urine with crystalloids or a change in the composition of the urine which lessens its solvent power. Bacterial infection does not seem to hold the same causal relation to nephrolithiasis that it does to cholelithiasis, although undoubtedly it may favor the growth of stones after they have been formed by causing ammoniacal decomposition of the urine and in consequence a rapid deposition of phosphates. Some authors regard abnormal mobility of the kidney as an important predisposing factor. Recent observations have failed to support Ebstein's view, formerly accepted, that a nucleus of organic material is essential to crystallization.

**Results.**—(1) Stones may remain in the pelvis of the kidney, and by their presence excite *pyelitis* or *pyelonephritis*, which in turn may lead to *ureteritis*, or, more rarely, to *perinephritic abscess*. Occasionally they are unattended by any obtrusive symptoms, and give rise to no other local lesion than a moderate grade of *hydronephrosis*. Even large dendritic calculi may thus remain quiescent for an indefinite period. In rare instances a *malignant growth* in the renal pelvis is excited by the presence of a calculus.

2. Stones very frequently enter the ureter and thereby produce attacks of *renal colic*. From the ureter they may again fall back into the pelvis of the kidney, or they may pass onward into the bladder and ultimately escape from the body in the urine. According to Braasch,[1] probably 75 per cent. of renal stones pass spontaneously within a few months following the first symptom. Occasionally a stone remains in the bladder and becomes the nucleus of a *vesical calculus*. In many cases stones become *impacted in the ureter*. Of 654 cases of lithiasis of renal origin operated on at the Mayo Clinic stones were found lodged in some portion of the ureter in 230 (Braasch and Moore[2]). Both ureters are obstructed in about 6 or 7 per cent. of all cases of ureteral lithiasis. Impaction may occur at any part of the ureter from the pelvic junction to the vesical orifice, but the most frequent site is some point in the lower third of the duct. If the occlusion is sudden, complete and permanent, the corresponding kidney, owing to the great pressure of urine, is likely to undergo atrophy; if it is of gradual development, incomplete or intermittent, hydronephrosis or pyonephrosis usually results. Other sequels of persistent impaction are ulceration of the ureter, sometimes with recurring hematuria, and stricture of the ureter. In 1911 Frenkel[3] found recorded 25 cases in which calculi had escaped through the wall of the ureter into the pelvis.

**Symptoms.**—Pain in the lumbar region is the most constant symptom of stone in the kidney. It may be severe or merely a dull ache, and paroxysmal or continuous with exacerations. In many cases it is localized in the costovertebral angle, but not rarely it radiates downward to the bladder, testicle, penis or thigh. Other radiations may be over the entire back, to the lower right abdominal quadrant, upward toward the liver, along the course of the sciatic nerve, and to the opposite renal region. The paroxysms or exacerbations of pain often directly depend upon physical exertion, but may occur during absolute repose. Occasionally there is no pain, the chief subjective manifestation being vesical irritability or dyspepsia with attacks of nausea and vomiting. The tendency to micturate frequently is, as a rule, more pronounced during the day than at night. Palpation sometimes elicits tenderness over the affected kidney, and if there is any considerable degree of hydronephrosis or pyonephrosis, or if the stone is of great size, it may reveal also a definite tumor. Not rarely deep percussion over the loins causes pain when pressure is without effect (Jordan Lloyd's sign).

[1] Minnesota Med., 1920, iii, 387.
[2] Jour. Amer. Med. Assoc., Oct. 9, 1915.
[3] Annal. des Mal. des Org. Génito-urinaires, 1911, xxix, No. 20.

Blood and pus are found in the urine in the majority of cases, but frequently only on microscopic examination. Gross hematuria, however, occurs in about 50 per cent. of the cases and occasionally the bleeding is profuse. Crystals of uric acid, calcium oxalate, etc. are sometimes present in the urinary sediment, and not rarely the urine contains also a trace of albumin and a few hyaline casts as the result of renal irritation. In from 5 to 10 per cent. of the cases the urine is normal in every respect.

Roentgen-ray examination in skilful hands yields positive results in about 85 per cent. of the cases and should be made whenever urinary lithiasis is suspected. Preparatory to the examination, which should include the entire tract on both sides, food should be withheld for nearly 24 hours and the bowel should be unloaded by a brisk purgative (Pancoast). Stones may be missed if the patient is very stout or if they are hidden behind bony parts; on the other hand, shadows suggestive of renal stones may be produced by gall-stones, foreign bodies in the intestine, phleboliths in the veins, dark moles on the back or calcified mesenteric lymph-nodes. Pyelography is sometimes useful in rendering a stone visible that has been invisible in the ordinary roentgenogram, as well as in determining the exact position of the stone and the extent of the renal damage.

*Ureteral Calculi.*—A stone may be present in the ureter for weeks or months without producing any symptom whatever; more frequently it gives rise to pain in the renal region or to typical renal colic. In other cases pain is referred to one of the other abdominal organs, such as the appendix, gall-bladder, stomach, intestine or ovary, or is indefinitely distributed over the abdomen. Vesical irritation is common and may be the dominant feature, especially if the impaction is near the bladder. Red blood corpuscles and pus cells are present, as a rule, in the urine. Gross hematuria is much less frequent than in renal stone.

Anuria may occur in consequence of unilateral ureteral obstruction if the other kidney is absent or more or less diseased. Whether it can occur as the result of a reflex inhibition of the function of a perfectly sound kidney on the side opposite that of the obstructed organ, as Imbert, Israel, Rovsing and others have supposed, is doubtful. Complete suppression also occurs, of course, when both ureters are completely occluded. When persistent, anuria is followed by the asthenic form of uremia, which is manifested by progressive weakness, attacks of vomiting, emaciation and coma.

Occasionally, a stone in the lower ureter can be palpated through the vagina or the rectum. Roentgenographic studies are invaluable, although they are negative somewhat more frequently in ureteral than in renal lithiasis. Sometimes ureteral calculi that are missed in ordinary roentgenograms are revealed in stereoscopic plates or in roentgenograms that are made after the introduction of an opague ureteral catheter or during the injection of thorium solution into the ureter. Cystoscopy itself is useful. It shows which ureter is functioning normally and makes the diagnosis certain in the comparatively rare cases in which the stone is lodged at the vesical meatus. Occasionally, a stone in the ureter may be detected by the scratch marks it makes on a wax-tipped catheter.

*Renal Colic.*—The attack of colic frequently follows muscular effort, although it may come on during complete repose. The pain, which is often violent and marked by exacerbations and remissions, usually radiates from the kidney down the ureter to the bladder, and thence to the urethra or to the testicle and thigh of the same side. In typical cases the testicle is forcibly retracted, and if the attack proves obstinate, it may become swollen and tender. In some cases the pain radiates in all directions around the body,

to the chest and even to the shoulder. Occasionally, it is referred to the opposite kidney. The attack is usually accompanied by nausea and vomiting, profuse perspiration, pallor and prostration. More rarely it is acccompanied by a chill and an elevation of temperature. While the pain continues there may be a frequent desire to urinate, although the quantity of urine is, as a rule, much diminished. Unless the ureter is completely obstructed, the urine is usually mixed with blood and mucous.

The duration of an attack of renal colic varies from a few minutes to several days. Cessation of pain does not necessarily mean that the stone has entered the bladder or has fallen back into the pelvis of the kidney, for it sometimes occurs with ureteral impaction. The close of the attack is frequently marked by free urination and the passage of gravel or of the calculus itself.

**Diagnosis.**—When accompanied by pain in the loin, radiating to the testicle and thigh, attacks of colic precipitated by exertion, persistent local tenderness, hematuria, and the presence of crystalline fragments in the urine, nephrolithiasis can scarcely fail of recognition. In very many cases, however, owing to the indefiniteness of the symptoms or their close resemblance to other morbid conditions the diagnosis may be difficult. *Movable kidney, tuberculosis of the kidney, malignant tumor of the kidney, cholelithiasis, ovarian disease, appendicitis, crises of tabes dorsalis, vesical calculus, seminal vesiculitis, arthritis of the spine* and *sacro-iliac strain* at times present symptoms very similar to those of renal calculus. In every instance all the available evidence should be carefully weighed before a definite opinion is given. X-ray examinations of the entire tract are indispensable, and, if necessary, should include stereoscopic pictures, pyelograms, ureterograms, etc. and be supplemented by the passage of a wax-tipped ureteral catheter. The differential diagnosis between nephrolithiasis and *tuberculosis of the kidney* may be especially difficult. In the latter the family and personal history, evidences of tuberculosis in other organs, and the detection of tubercle bacilli in the urine are important diagnostic points. The persistence of hematuria after the patient has been at rest, fever with recurring chills, pronounced hyperemia and tumefaction about the ureteral orifice upon cystoscopic examination, and negative results with roentgen rays also suggest tubercle. In obscure cases recourse should be had to the tuberculin test and the injection of a portion of the urinary sediment into the peritoneum of a guinea pig.

Renal colic due to stone must be distinguished from other conditions causing paroxysms of abdominal pain, such as biliary colic, Dietl's crises occurring in movable kidney, mucous colitis, appendicitis, and lead colic. In *biliary colic* the pain is usually in the epigastrium or right hypochondrium and radiates around the chest or to the right scapula, the gallbladder is often tender and enlarged, jaundice sometimes follows the attack, frequency of micturition is not observed, and the urine is free from blood, mucus, etc. The diagnosis of *Dietl's crises* depends mainly on the detection of a floating kidney, although it must be borne in mind that nephroptosis and nephrolithiasis not rarely coexist. In some instances the pain in *mucous colitis* is sufficiently severe to suggest the occurrence of renal colic. Examination of the stools, however, should soon lead to the recognition of the real nature of the condition. When the pain of renal colic is referred to the lower right abdominal quadrant it may be difficult to exclude *appendicitis*. In the latter, however, the pain is usually accompanied by localized tenderness and muscular rigidity, leucocytosis is almost always present, vesical disturbances are uncommon, and the urine remains free from blood, mucus, etc.

Fever is less helpful; it is sometimes absent in appendicitis and it may be present in renal colic. In *lead colic* the blue line on the gums, the obstinate constipation, the basophile stippling of the red blood cells and the absence of vesical and urinary symptoms, together with the history of occupation or habits will usually suffice to establish an accurate diagnosis.

**Prognosis.**—In the early stages of the disease the prognosis as to life is favorable. Only in rare instances are such symptoms as renal colic or hematuria severe enough to prove fatal. Even after complete recovery, however, a tendency to relapse remains. Septic infection of the kidney (pyonephrosis or pyelonephritis) or any pronounced impairment of the function of both kidneys, as shown by modern tests, adds very much to the gravity of the condition. Calculous anuria is an extremely dangerous complication, and unless relieved results in death usually within a week or ten days.

**Treatment.**—Stones once formed in the kidney cannot be dissolved, but appropriate medical treatment may be successful in preventing the formation of fresh deposits and in flushing out small concretions. As the conditions that favor the production in excess of uric acid, calcium oxalate, etc., and the precipitation of these substances in the pelvis of the kidney are only imperfectly understood, it is not possible to meet exactly the causal indication. However, if the urine is decidedly acid it is advisable to restrict the amount of meat in the diet and to forbid the use of foods rich in nuclein, such as liver, brain, kidney, fish roe, meat extracts, etc., as well as fancy dishes of all kinds, alcoholic beverages, and tea and coffee in excess. Irrespective of the character of the stone, much benefit often accrues from abundant water-drinking between meals. This not only favors the expulsion of small concretions, but by diluting the urine, it also tends to prevent the precipitation of the crystalloids. If the urine is highly acid the water may be made alkaline by the addition of potassium citrate—1–1½ dr. (4.0–6.0 gm.) to the quart (1.0 L). As a rule, about a quart of such water should be consumed in the twenty-four hours. Some precaution is necessary not to allow the urine to become too alkaline, since this may lead to a deposition of phosphates about the primary calculus. Alkaline mineral waters, such as Carlsbad, Vichy, Vals, Contrexville, etc., have been extensively employed, but they are less efficacious than plain water that has been rendered alkaline by the addition of potassium citrate.

Certain special remedies have been brought forward as solvents of uric acid, namely, piperazin, lycetol, piperidin tartrate and quinic acid in combination with lithium (urosin) or piperazin (sidonal). While some authorities claim to have obtained good results from these drugs, the majority of unprejudiced observers are sceptical as to their merits. Hermann, Casper, and others have spoken favorably of glycerin—1 to 3 ounces (30.0–90.0 mils) in water between meals and repeated two or three times in several days. Hexamethylenamin is of service in warding off infection, but it is only effective in acid urine.

Since phosphatic calculi can be deposited only from alkaline urine the indication is to render the urine acid, a task not always easy of accomplishment. Among remedies recommended for the purpose, the best are acid sodium phosphate and benzoic acid. Unfortunately, the continued use of these drugs is prone to cause indigestion, an effect which detracts materially from their value.

In the milder cases of nephrolithiasis without evidence of renal infection, a sojourn at one of the well known spas, such as Carlsbad or Contrexville on the continent of Europe, Harrogate in England, and Bedford in America,

is often beneficial, the good effects being due, however, more to the freedom of business cares and worries, the regular life and the regime than to any special ingredient of the waters.

*Renal Colic.*—The indications are to relax the ureteral spasm and to relieve the pain. These are best fulfilled, as a rule, by hypodermic injections of morphin—$\frac{1}{4}$ grain (0.016 gm.) and atropin—$\frac{1}{150}$ grain (0.0004 gm.), repeated as often as necessary, the effects of the drugs being carefully observed. A hot bath (100°–110° F.) or the use of hot fomentations locally is also of service. Warm diluents should be given freely. In very severe cases inhalations of chloroform are sometimes necessary. In mild attacks benzyl benzoate in doses of 20 drops of a 20 per cent. solution by the mouth, repeated in half an hour or an hour, may suffice. After the attack the urine should be examined after every act of micturition to see if the stone appears.

**Surgical Treatment.**—In many cases surgical intervention affords the only hope of permanent relief. Operation is demanded when attacks of colic occur with such frequency as to prove disabling, when there are evidences of infection, and when there is persistent obstructive suppression of urine, provided, of course, that the various tests do not show such a reduction in the functional capacity of the kidneys as to render the risk of operation too hazardous. If multiple stones are present, even if the individual stones are small, and only one kidney is involved operation is usually indicated, but in bilateral nephrolithiasis, with multiple calculi, operation is, as a rule, inadvisable.

In renal calculus pyelotomy, nephrotomy or nephrectomy will be the operation of choice according to the size, shape and location of the stone, and the condition both of the affected kidney and its fellow. The operative mortality in aseptic cases is less than 5 per cent., in infected cases it is 20 per cent. or more. Owing to the great likelihood of small ureteral stones being finally passed, expectant treatment should be given a thorough trial in all uncomplicated cases. According to Braasch and Moore,[1] it is, as a rule, advisable to wait at least three months until nature has made several attempts to dislodge the stone. Kidd[2] believes that unless there are imperative indications for operative measures it is safe to wait one or two years, as the kidney may recover sufficiently to do much useful work even if the ureter has been partially blocked for a much longer period. In large proportions of cases simple catheterization of the ureter or dilatation of the lower ureter is followed by the passage of the stone. Not rarely the injection of sterile oil or of 5 mils of 4 per cent. solution of papaverin into the ureter serves to release the calculus. Anuria, unless relieved within 24 or 36 hours by hot applications to the lumbar regions, water in abundance, alkaline diuretics, intestinal irrigation with normal salt solution at 110° F., etc. demands surgical intervention.

## HYDRONEPHROSIS AND PYONEPHROSIS

*Hydronephrosis* is the term applied to dilatation of the pelvis and calyces of the kidney, with atrophy of the secreting tissue, the result of some impediment to the urinary outflow and the accumulation of a non-purulent fluid. If the pelvis of the kidney is distended with pus or pus and urinous fluid, the

[1] Jour. Amer. Med. Assoc., Oct. 9, 1915.
[2] Brit. Med. Jour., July 31, 1920.

condition is known as *pyonephrosis*. In either process both kidneys or only one may be involved.

**Etiology.**—Hydronephrosis may be congenital or acquired. The congenital form, which in the majority of cases is bilateral, may be due to atresia of any part of the urinary channel, an abnormal insertion of the ureter into the renal pelvis, or compression of the ureter by an anomalous artery. The aquired form is usually caused by ureteral obstruction the result of an impacted calculus, cicatricial stricture, angulation or torsion of the ureter of a movable kidney, or compression from without by morbid growths or inflammatory bands. Occasionally, a gravid uterus compresses one or both ureters. Rarely a tumor within the bladder or the ureter itself impedes the escape of urine. Finally, a moderate degree of renal distention may be brought about by obstruction of the urethra from stricture, an enlarged prostate, or even phimosis. Hydronephrosis is most readily induced when the obstruction develops gradually and is incomplete or more or less intermittent. Sudden obstruction, especially if complete and persistent, usually inhibits the secretion of urine (Albarran) and leads to extreme atrophy of the kidney (Cohnheim).

Pyonephrosis may result from secondary infection of the sac in simple hydronephrosis or from retention of the pus in pyelonephritis. Bilateral pyonephosis is common in cases of prostatic enlargement with chronic cystitis.

**Morbid Anatomy.**—All degrees of renal distention are observed. In extreme cases the pelvic sac may contain several quarts of fluid, which in hydronephrosis is at first urinous, but later serous or gelatinous, and which in pyonephosis is pus or pus and urinous fluid in varying proportions. As the distention increases the substance of the kidney becomes more and more atrophied until finally the organ is transformed into a large multilocular cyst. In pyonephrosis the lining of the cyst is often ulcerated or incrusted with urinary salts, especially phosphates. Renal distention is frequently accompanied by more or less dilatation of the ureter (hydro-ureter or pyo-ureter).

**Symptoms.**—Hydronephrosis that is not sufficiently pronounced to produce a demonstrable tumor may exist without symptoms. In many cases, however, even a slight degree of renal distention gives rise to attacks of pain simulating renal colic due to calculus. After such attacks the urine may contain a trace of albumin and a few blood-corpuscles or even a few pus cells. In advanced cases a tumor develops in the region of the affected kidney. On palpation it is elastic and sometimes fluctuating. Not rarely it is movable with respiration. It may or may not be painful. Occasionally the tumor varies in size from time to time, its subsidence being marked in some instances by transitory polyuria and its return to former dimensions by more or less pain (intermittent hydronephrosis). Such cases usually, but not invariably, depend upon a movable kidney with kinking or twisting of the ureter.

The symptoms of pyonephrosis are in the main those of pyelonephritis (see p. 784). The constitutional evidences of suppuration—fever, chills, sweats, leucocytosis—are usually present, and, unless the obstruction is complete, the urine contains pus. In advanced cases a tumor with the characteristics of that of hydronephrosis appears in one or other loin.

**Diagnosis.**—Hydronephrosis may be confused with solid tumors of the kidney or adjacent organs, cysts of the kidney, sarcoma of the retroperitoneal lymph-nodes, large ovarian cysts, and even ascites. In excluding these conditions one must rely mainly upon the etiologic factors in the case, the physical peculiarities of the tumor and the direction of its growth, and

repeated examinations of the urine. Marked variations in the quantity and composition of the urine, especially if accompanied by changes in the size of the tumor, are of great significance. Cystoscopic examination may aid in the diagnosis by revealing a persistent absence of urinary flow through one or other ureteral orifice, and ordinary roentgen-ray examinations are of service in demonstrating the presence or absence of ureteral concretions, but usually roentgen-ray examinations after ureteral catheterization and injection of the renal pelvis with an opaque medium, such as a solution of sodium bromid or thorium nitrate or a suspension of colloidal silver (pyelography) supply the most direct evidence, especially in early cases.

It is not always possible to distinguish between pyonephrosis and suppurative pyelonephritis without renal stone, but the exact differentiation is not important, as the treatment of the two conditions is virtually the same.

**Treatment.**—This must be directed to the cause of the obstruction and retention. In many cases the treatment is essentially surgical, nephropexy, a plastic operation on the ureter or pelvis, nephrostomy or nephrectomy being required according to the cause and the character of the renal distention.

## TUMORS OF THE KIDNEY

Benign tumors, chiefly lipoma, fibroma, papilloma and adenoma, are found in the kidney, but they are comparatively rare and have little clinical significance. Malignant tumors are not uncommon and include sarcoma, carcinoma and so-called hypernephroma. **Sarcoma** occurs especially in young children, although it may be observed in adults. Of 219 cases of malignant tumor of the kidney in children collected by Steffen[1] 168 (76 per cent.) occurred in the first 5 years. Histologically, these tumors consist of spindle cells, round cells, smooth or striated muscle-cells and abortive tubules and glomeruli in varying proportion. They grow rapidly and attain a large size, sometimes filling one-half or two-thirds of the abdominal cavity. In many cases they become cystic. Occasionally, even before birth a renal sarcoma is so large that it interferes with the delivery of the child. Extensions to adjacent organs and metastases are not common, but the latter may occur in the liver and lungs.

**Carcinoma** is probably the most common tumor of the kidney, although it is often atypical and difficult to differentiate from the so-called hypernephroma. It usually appears in the form of adenocarcinoma (papillary or alveolar). Squamous-cell epithelioma, however, is occasionally found in the pelvis of the kidney. Of 47 cases of papillomatous epithelioma of the renal pelvis analyzed by McCown,[2] 10 were associated with stone in the kidney. In many cases the tumor of the kidney attains a large size and destroys most of the kidney. Invasion of the renal veins, the ureters, and adjacent organs occurs at an early period, and metastasis to the regional lymphnodes, lungs, liver and bones is very frequent. In papillary epitheliomas of the renal pelvis metastasis to the bladder is common (17 of McCown's cases).

**Hypernephroma.**—Birch-Hirschfeld applied this name to the group of renal tumors described in 1883 by Grawitz[3] and regarded by him as derivatives of particles of adrenal tissue aberrant in the cortex of the kidney.

[1] Die malig. Geschwulste im Kindersalter, 1905.
[2] Jour. Amer. Med. Assoc., Oct. 30, 1920.
[3] Virchow's Archiv., 1883, xciii, 39.

These tumors occur chiefly in persons between 40 and 60 years of age, and are much more frequent in men than in women. As a rule, they develop just beneath the capsule of the kidney, are vascular and fatty, and in the early stages are sharply circumscribed. Much difference of opinion exists regarding the origin and classification of such growths, but recent studies seem to have demonstrated that many members of the group are really derived from renal epithelium and are of an adenomatous or adenocarcinomatous nature (renal hypernephroma), while others are, as Grawitz believed, derived from adrenal rests (adrenal hypernephroma). Being of mesothelial origin, true adrenal rest tumors are also known as mesotheliomas. Morphologically and clinically, they may have adenomatous, carcinomatous, or sarcomatous properties. Many of them are frankly malignant, while others grow slowly and show little tendency to metastasis. Although usually single, they may be multiple, and sometimes they are found in both kidneys. In the malignant form metastases are often widespread, but the lungs, liver, bones, renal veins, and vena cava are involved most frequently. Occasionally, metastases appear so early, especially in the bones, that they are mistaken for primary tumors.

**Symptoms.**—*Pain* in the back or abdomen is rarely absent and in many cases it is the first indication. It may be a mere dragging sensation or sharp and lancinating. Not infrequently it presents the features of renal colic. *Hematuria* occurs at some time in the course of the disease in two-thirds of the cases. It was the primary symptom in 36 per cent. of 83 cases reported by Braasch[1] and in 26.9 per cent. of 59 cases reported by Willan.[2] The bleeding may be persistent or intermittent. Clots in the ureter are probably responsible for the colicky pains. In addition to blood the urine may contain more or less pus. In a few instances fragments of the tumor have been discovered in the urinary sediment. *Cachexia*—pallor, weakness and emaciation—supervenes sooner or later in the majority of cases. A *tumor* is revealed by palpation in about 80 per cent. of the cases, but it is sometimes impossible to determine by the hand alone that the kidney is the organ affected. The mass is often movable, and in exceptional instances it is pulsatile. The colon lies in front of it. Enlargement of the superficial veins, varicocele, ascites and even edema of the legs sometimes occur as a result of pressure upon large venous trunks or of direct invasion of the vena cava.

The abnormal development of the secondary sex characteristics, which frequently accompany adrenal growths (adrenal hypernephromas) in children are never observed in Grawitz' tumors of the kidney (Glynn).

**Diagnosis.**—Renal tumors are readily mistaken for polycystic kidney and retroperitoneal tumor. In *polycystic kidney* the renal enlargement can frequently, but not invariably, be felt on both sides, the course is usually more protracted, and the functional activity of the kidneys as determined by chemical tests is more often diminished. *Retroperitoneal tumor* is frequently indistinguishable. Complete fixation of the mass and absence of hematuria, however, are suggestive. Other conditions that must be excluded are *hydronephrosis*, *pyonephrosis*, and *tumors of adjacent organs*. Important diagnostic data are obtained from bowel inflation, cystoscopy, ureteral catheterization, and roentgenographic studies, including pyelography. The occurrence of papillary tumor of the bladder in association with unilateral hematuria is highly suggestive of pelvic epithelioma.

**Course, Prognosis and Treatment.**—Left to themselves, tumors of the

[1] Jour. Amer. Med. Assoc., Jan. 25, 1913.
[2] Brit. Med. Jour., Nov. 27, 1915.

kidney always prove fatal. The duration varies from a few months to several years. Occasionally hypernephomas remain dormant for long periods, and then become active. Nephrectomy offers the only hope of cure. The mortality of the operation itself in renal tumor is from 18 per cent. (Braasch) to 20 per cent. (Rovsing). According to Braasch,[1] of 51 patients in whom nephrectomy for renal tumor was successfully done 37 per cent. were alive 3 years or longer, and according to Paschen[2] of 268 patients treated surgically for hypernephroma 17.7 were alive at the end of 3 years. Hyman[3] reports 20 nephrectomies for hypernephroma with an operative mortality of 5 per cent. and survival of 33.3 per cent. of the patients for a period of 3½ years or longer.

## CONGENITAL POLYCYSTIC KIDNEY

Small cysts are frequently found in the cortex of the kidney in renal sclerosis. They are probably retention cysts which have been produced by constriction of the uriniferous tubules. Single large cysts are occasionally found in otherwise healthy kidneys. They are probably the result of accidental occlusion of the tubules. In total hydronephrosis the kidney may be transformed into a huge cyst. Again, echinococcus cysts and dermoid cysts may occur in the kidney. All of these conditions are distinct from the polycystic kidney. In the latter the viscus is enlarged and studded with numerous cysts varying in size from a hemp seed to an orange. The cysts are lined with epithelium and are filled with a clear or turbid fluid, in which traces of the urinary constituents may usually be detected.

In the large majority of cases both kidneys are involved. Of 88 cases collected by Ritchie,[4] in only two was the disease unilateral. In more than one fourth of the cases cysts are also found in other organs, especially the liver (Lejars[5]), and not infrequently abnormalities of development, such as cleft palate, harelip and spina bifida, are also present. The disease is probably always congenital, although in many cases it remains quiescent until late in life. The kidneys are sometimes so large at birth as to interfere with labor. Fussell[6] cites 11 cases in which it was necessary to multilate the fetus before delivery could be effected. Steiner, Borelius, Osler and others have reported cases in which the condition was distinctly hereditary. The formation of cysts has been explained in various ways. Virchow attributed them to stenosis of the tubules, the result of prenatal inflammation. Goodhart suggested that they were neoplasms— cystic adenomas. The most plausible theory is that advocated by Shattock which refers them to faulty development or misplacement of embryonic remnants.

**Symptoms.**—Children who survive birth with the disease well developed usually succumb early to the effects of pressure or uremia. In adults cystic kidney may remain latent for an indefinite period, and not rarely it is discovered only at autopsy. In many cases, however, there are definite symptoms referable to the kidneys. Dull pain in the loins or abdomen may or may not be present. The urine is usually increased in amount and of low specific

[1] Jour. Amer. Med. Assoc., Jan. 25, 1913.
[2] Archiv. f. klin. Chirurg., 1915, cvii, No. 2.
[3] Surg., Gynec. and Obstet., 1921, No. 3, 216.
[4] Laboratory Rep. of the Roy. Col. of Physicians, Edinburgh, vol. iv.
[5] Du gros rein polykystique, Thèse de Paris, 1888.
[6] Medical News, Jan. 10, 1891.

gravity. It contains a small amount of albumin, hyaline or granular tube-casts, and almost invariably a greater or less number of erythrocytes. Actual hematuria is common and sometimes is preceded by severe pain, which is suggestive of renal calculus, and which is probably due to extreme distention of the cysts with blood. A tumor, unilateral or bilateral, is recognizable in a large proportion of cases. Occasionally the entire abdomen is enormously distended. Fluctuation, however, can rarely be elicited. In advanced stages of the disease arterial hypertension, cardiac hypertrophy, cachexia, diminished renal permeability, and uremia supervene, the clinical picture being virtually that of chronic glomerulonephritis. By measuring the 'phthalein excretion of the individual kidneys it is possible to determine in which organ the greater destruction of renal tissue has taken place. The disease eventually proves fatal in the majority of cases, death resulting from uremia, cardiac failure, cerebral hemorrhage or suppuration of the cysts. Chevassu[1] has collected 88 cases of suppuration in polycystic kidneys.

**Treatment.**—Although the disease is usually bilateral, surgical intervention is indicated in the presence of suppuration, persistent hematuria, mechanical obstruction, etc., unless functional tests give evidence of pronounced renal insufficiency. In 24 cases treated at the Mayo Clinic[2] unilateral nephrectomy was done in 14 with 2 deaths and Rovsing's operation, consisting of systematic puncture of the cysts through an incision in the loin, was done in 10 with 3 deaths.

## AMYLOID DISEASE OF THE KIDNEY

(Lardaceous or Waxy Degeneration of the Kidney)

Amyloid disease of the kidney is characterized by the appearance in the ground-substance of the bloodvessels and connective tissue of the organ of a peculiar albuminoid compound which yields a characteristic color reaction with iodin and various basic aniline dyes. Although its origin has not been definitely determined, amyloid material appears to be the product of an interaction between the tissue-juices and some abnormal substance dissolved in the blood. According to Krakow, it is a compound of chondroitin-sulphuric acid and a protein (histone).

**Etiology.**—Other organs, especially the spleen and liver, are usually involved at the same time as the kidneys, the underlying cause of the degeneration being some general, chiefly infectious, disease, accompanied by wasting and anemia. Tuberculosis of the bones, joints or lungs supplies the conditions most favorable to its development. Less commonly other protracted suppurative or ulcerative processes, such as those occurring in tertiary syphilis, chronic dysentery and actinomycosis, are responsible for it. Rarely it arises independently of suppuration in the cachexia of cancer, leukemia or malaria. Owing to the more successful treatment of suppurating processes in bones and joints, of tuberculosis and of syphilis, amyloid disease is much less common than formerly.

**Morbid Anatomy.**—The gross appearance of the kidney varies with the extent of the disease and the character of the accompanying lesions. In typical cases the organ is considerably enlarged, smooth, firm, anemic, and somewhat translucent, like par-boiled bacon. As a rule the pyramids are less affected than the cortex and retain their normal color. Iodin in the

[1] Jour. d' Urolog. Paris, 1921, No. 5–6, 373.
[2] Braasch, Surg., Gynec. and Obst., 1916, xxiii, 697.

form of a dilute aqueous solution[1] stains the amyloid areas mahogany brown and the surrounding tissue straw-yellow.

**Pathologic Histology.**—Sections intended for microscopic study are best treated with methyl-violet. This dye turns the amyloid material pink or red and the tissue violet-blue. The glomeruli are first attacked. In the early stage the capillary loops present only a few homogeneous, wax-like flakes, with a corresponding reduction in the number of nuclei. Later, the entire glomerulus may become transformed into a structureless disc. Eventually the degenerative process invades the minute arterioles and venules and also the basement membrane of the tubules. In the capillaries the amyloid substance is deposited immediately outside of the endothelial cells, and in the arterioles it appears first in the connective tissue of the media and then extends to the deeper layers of the intima. It does not affect either the endothelium or the epithelium. In addition to the amyloid infiltration itself, changes characteristic of chronic tubular nephritis and of renal sclerosis are more or less in evidence.

**Symptoms.**—The symptoms are not very characteristic. In typical cases the urine is abundant, light colored, of low specific gravity, and contains relatively a large amount of albumin. In addition to serum-albumin, globulin is often present in considerable quantity. The sediment is scanty and contains a few hyaline or granular casts. Casts with an amyloid reaction are scarcely ever observed.

When the disease is fully developed, pallor and weakness are usually prominent symptoms. Dropsy, moderate in degree, occurs in many cases, but it is a symptom of the general cachexia or concomitant nephritis, rather than of the amyloid disease itself. Obstinate diarrhea is a common complication. Unless the amyloid process is implanted on kidneys already the seat of chronic glomerular inflammation, the blood pressure remains persistently low and uremia, retinitis and cardiovascular changes very rarely occur.

**Diagnosis.**—The diagnosis is based on the character of the urine, especially copious watery urine containing a considerable amount of albumin; on the low blood pressure; on the demonstration of amyloid infiltration in other organs, in particular a smooth, painless enlargement of the liver and spleen; and on the presence of such a condition as cold abscess, ulcerative syphilis, etc., which predisposes to amyloid change. The diagnosis becomes more certain if at the same time marked cachexia, moderate edema, and persistent diarrhea are also present.

**Prognosis and Treatment.**—Amyloid degeneration is usually an irreparable condition, although an arrest of the process is possible when the primary cause can be removed. The treatment is mainly that of the underlying disease. Iodin preparations are usually recommended, but they are of doubtful utility.

## PERINEPHRIC ABSCESS

Suppuration of the fatty capsule of the kidney may follow (1) direct injury or violent muscular effort; (2) septic inflammation of the kidney itself (pyelonephritis, pyonephrosis, renal tuberculosis); (3) abscess of the abdominopelvic organs; (4) ulcerative lesions of the intestine (typhoid fever, appen-

[1] Gram's solution: Iodin, 1 part; potassium iodid, 2 parts; water, 300 parts—gives the best results.

dicitis, chronic dysentery); (5) acute infectious diseases. Occasionally the primary focus of suppuration is in the pleura or vertebræ. Of 230 cases collected by Küster,[1] 67 were due to traumatism and 59 to suppuration in the kidney. The majority of cases occur between the ages of 20 and 45, but the disease is not rare in children. It is twice as frequent in men as in women.

**Morbid Anatomy.**—The pus is usually situated between the kidney and the posterior abdominal wall. It may be yellow and odorless, or dark and putrid. Not rarely it has a feculent odor from contact with the colon. In many cases the abscess extends to the surface in the loin, but it may burrow downward and into the groin, or it may burst internally into the pleura, lung, intestine, vagina, etc. In some instances it remains intact and leads to death through septicemia. Very rarely the pus becomes inspissated and transformed into a caseous mass surrounded by a fibrous capsule.

**Symptoms.**—The onset is usually marked by deep-seated pain, which may be localized in the lumbar region, although it often radiates to the hip, iliac crest, thigh, knee or external genitals. The patient lies, as a rule, on the back with the thigh flexed, and in walking inclines the body to the affected side. The spine is abnormally rigid. The general phenomena of deep-seated suppuration, such as irregular fever, sweats, chills, pallor, leucocytosis and emaciation, are commonly present. Digestive disturbances—anorexia, vomiting, flatulence, and constipation or diarrhea—frequently occur and not rarely there is more or less cough. When the kidney is the seat of the primary lesion the urine contains pus, blood and albumin, but in other cases it may be normal.

Physical examination reveals tenderness in the lumbar region, increased muscular resistance, and eventually, in the majority of cases, a tumor. Occasionally the tumor does not appear until the abscess has reached a large size. On bimanual palpation a mass may be outlined, which is tender on pressure. Fluctuation is rarely detected. As the abscess approaches the surface, the skin over it becomes tense, red and edematous. In a few instances pressure on the iliac veins has resulted in swelling of the foot and ankle. Occasionally tumefaction is the only symptom.

**Diagnosis.**—Careful study of the clinical history, physical signs and condition of the urine and blood will generally suffice to establish the diagnosis. In *pyonephrosis* the swelling is usually less diffuse, the pain more paroxysmal, the tenderness in the back less constant, the characteristic posture absent, and the urine, as a rule, contains an abundance of pus. *Malignant tumors of the kidney* are, as a rule, more circumscribed, often present an irregular surface, usually cause hematuria, and are unattended by fever and other symptoms of suppuration.

In *hip-joint disease*, which is sometimes simulated when the pain is referred to the knee, passive motions of the hip-joint cause pain, tenderness and swelling occur over the upper end of the femur and are absent over the kidney, and the leg on the affected side is often shortened.

**Treatment.**—This consists in evacuating the pus and draining the abscess cavity. The mortality is greatly increased by delay in operating. In Küster's 230 cases it was 34 per cent., but in 35 cases seen by M. Miller[2] it was only 14.3 per cent. and in Gibney's[3] 28 cases of primary nature occurring in children there were no deaths.

[1] Die Chirurg. der Nieren, der Harnleiter und der Nebennieren, Stuttgart, 1896–1902.
[2] Annals of Surg., March, 1910.
[3] Chicago Med. Jour., 1880, xl, 561.

# INDEPENDENT DISEASES OF THE BLOOD-FORMING ORGANS AND THE ANEMIAS

## BLOOD-FORMING ORGANS

In adults the red blood-corpuscles are formed in the red marrow of bones. Their progenitors (erythroblasts) are nucleated and colorless. These cells multiply and the daughter cells take on hemoglobin and lose their nuclei, becoming erythrocytes, in which form they enter the blood-stream. When hemopoiesis is accelerated, as after severe hemorrhages and in certain pathologic conditions, red cells still retaining their nuclei (normoblasts) may escape prematurely into the circulating blood. In the fetus red blood-corpuscles are produced in organs other than the bone-marrow, notably in the liver and spleen, and in adults under stress of great need, as in severe anemias, these organs may again take on their hemopoietic function.

As to the origin of the different forms of white blood-corpuscles there is much diversity of opinion. Most hematologists, however, incline toward Ehrlich's view that the lymphocytes are supplied in large part, if not wholly, by the lymphoid tissues of the body, and that the granular forms, including the polymorphonuclear neutrophiles, eosinophiles and mast cells, are the descendants of mononuclear bone-marrow cells (myeloblasts). Concerning the origin of the large mononuclear leucocytes of the circulating blood nothing definite is known, although most authors believe that they are also derived from the bone-marrow. It is doubtful whether any of the circulating lymphocytes in health are formed in the bone-marrow, although it is possible that a few of them may have this origin. In certain diseases, however, the lymphoid cells of the marrow may proliferate to such an extent as to push aside all the other cells. While the source of the blood-plates has not been definitely determined, the hypothesis of J. H. Wright that they are detached processes of the giant cells (megakaryocytes) of the bone-marrow has found general acceptance.

Within certain limitations, pathologic agents, stimulating or destructive in their effect, may be specific, and exert their influence almost wholly on either the erythroblastic or the leucoblastic function, nevertheless, there is considerable evidence to show that influences which usually act on but one of the blood-forming tissues, may at times affect the whole hemopoietic apparatus. This is probably the explanation of the atypical blood-pictures that are not rarely observed in leukemia and also of the apparent combinations of leukemia with pernicious anemia (leukanemia).

No classification of the independent diseases of the blood-forming organs will be found satisfactory until one can be devised which shall be based upon a clear understanding of the etiologic factors involved, and a full knowledge of the origin and function of all the cellular forms present in the bone-marrow and lymphoid tissues, and the relation of these forms to the different varie-

ties of circulating leucocytes. The following provisional classification arranged by MacCallum, and based on Sternberg's grouping, is perhaps as logical as our present knowledge will allow and may be used for clinical purposes:

A. Hyperplasia of lymphoid tissues:
  (*a*) With leukemic blood:
    1. With swelling of lymphoid and lymphoid infiltration of organs..... *Chronic lymphoid leukemia; acute lymphoid leukemia.*
    2. With tumors originating in various situations and invading tissues..... *Leukosarcoma; (chloroma).*
  (*b*) Without leukemic blood:
    3. With tumors involving bone-marrow..... *Lymphoid or plasma-cell myeloma.*
    4. With general swelling of lymphoid tissue..... *Pseudoleukemia.*
    5. With regional invasive tumor-like growth..... *Lymphosarcoma.*
    6. With stigmata of general maldevelopment..... *Status lymphaticus.*
B. Hyperplasia of myeloid tissue:
  (*a*) With leukemic blood:
    7. With myeloid infiltration of organs..... *Myeloid leukemia; myeloblastic leukemia.*
    8. With tumors of the myeloid tissue..... *Chloromyelosarcoma (myeloid chloroma).*
  (*b*) Without leukemic blood:
    9. With tumors of the myeloid tissue..... *Myeloid myeloma.*
C. (Included here though probably not related). Tumor-like swelling of lymph-glands, with nodules in spleen, liver, lungs, etc., granulomatous alteration of lymphoid tissue of specific morphology, apparently infectious in origin..... *Lympho-granulomatosis or Hodgkin's disease.*

## LEUKEMIA

(Leucocythemia)

Leukemia is a disease of the blood-forming organs characterized by hyperplasia of the leucoblastic tissues and a marked increase in the number of leucocytes in the circulating blood. Two main types are distinguished, one in which the hyperplasia affects especially the myeloid tissue and results in a large number of circulating myelocytes—*myeloid leukemia*, and another in which the hyperplasia affects, especially the lymphoid tissues and results in a large number of circulating lymphocytes—*lymphoid leukemia*. In either case the process may be acute or chronic.

**Etiology.**—Although leukemia is not a very rare disease, it is a somewhat infrequent one. Nothing definite is known as to its cause. Of the chronic forms the majority of cases occur between the ages of 20 and 50 and of the acute forms the large majority are in the childhood and youth. Males are much more often attacked than females. Inheritance, unsanitary conditions, antecedent infection, and traumatism apparently have no etiologic influence. On the one hand, the disease appears to be related to the infectious processes and on the other, to the tumor formations. The case reported by Obrastzow in which a nurse became affected after caring for a leukemic patient and a similar one reported by Cabot have been quoted in favor of the theory of infection, and the reports of 3 cases of lymphatic leukemia in x-ray workers and of 1 in a chemist engaged in the preparation of radium, collected by von Jagic,[1] have been quoted in favor of the view that leukemia is a form of malignant neoplastic disease.

[1] Berlin. klin. Woch., 1911, xlviii, 1220.

## CHRONIC MYELOID LEUKEMIA

**Morbid Anatomy.**—The most conspicuous change is in the *spleen*, which is greatly enlarged, sometimes weighing as much as 6000 grams, or more. The organ is normal in shape, firm, and often adherent to the diaphragm and abdominal wall. Infarcts are common. On section, the pulp is grayish-red and the follicles are indistinct. Microscopically, the capillaries and intervening spaces are distended with myelocytes of all kinds, together with some erythrocytes and erythroblasts. The reticulum is more or less increased. The *liver* is considerably enlarged and, as a rule, pale. Microscopically, the capillaries are crowded with myelocytes, and collections of these cells, sometimes even small tumor-like masses of them, are also observed between the liver cells, which in consequence often undergo pressure atrophy. The other organs macroscopically show only the effects of anemia, but microscopically they almost always show, in addition, more or less myeloid infiltration, both circumscribed and diffuse. The changes in the *bone-marrow* are especially important. The marrow of the long bones instead of being fatty is firm, opaque and of a yellowish-gray or pinkish-gray color. Microscopically, the striking feature is the presence of an enormous number of myelocytes of all kinds. The *lymph-nodes* throughout the body are of normal size or slightly enlarged, the enlargement being due to adventitious cells, chiefly myelocytes.

The blood in the heart and large vessels is usually clotted, the coagula, owing to the large number of leucocytes, sometimes presenting a peculiar whitish or greenish (pus-like) hue—a finding which suggested to Virchow the term leukemia. Visceral and other hemorrhages are common, and ascites, due to pressure of the enlarged spleen, to anemia, or to leukemic infiltration of the peritoneum, may also be found.

The nature of the process is obscure. There is good reason for supposing, however, that the bone-marrow is primarily at fault, and that in response to some unknown stimulus there is an overproduction of leucocytes, with an output of many immature forms, and at the same time increased facilities for the discharge of the new cells into the circulating blood. Whether the myeloid accumulations in the liver, spleen and other organs are formed by increasing deposition from the blood, by mitotic proliferation of leucocytes already present, or, as many believe, by true myelocytic metaplasia or transformation of fixed cells *in loco*, is not definitely known.

**Symptoms.**—The onset is usually insidious, and often for many months there are no subjective symptoms or serious disturbances of nutrition, even though the blood changes are characteristic. In some cases the disease is discovered casually in an examination undertaken for some complaint unrelated to the leukemia and in other cases the patient first seeks advice on account of abdominal enlargement or tumor, pain in the side, increasing weakness, or hemorrhage. Anemia is not an early feature, but as the disease advances it becomes more or less marked and toward the end symptoms referable to it, such as dyspnea, palpitation, dizziness and edema, may dominate the picture. The anemia may be due to hemorrhages or to pressure atrophy of the erythroblastic tissue in the bone-marrow. Hemorrhages from various parts are common at all periods, epistaxis being the most frequent. In two of Osler's cases fatal hematemesis occurred before there was any evidence of existing leukemia. Symptoms referable to the digestive tract, such as flatulence, nausea, vomiting, diarrhea, etc., are often troublesome features. Periods of irregular fever occur from time to time in virtually all cases. Defective vision and disturbances of hearing from hemorrhages or leukemic infiltrations in the fundus of the eye or internal ear respectively sometimes occur. Persistent priapism is not rarely observed and may appear

early. It is usually due to thrombosis in the corpora cavernosa and in several instances it has been relieved by incision and evacuation of the clots. Pain over the bones with tenderness is an occasional symptom. Toward the end of the disease asthenia, emaciation and dyspnea are prominent features, the last resulting from anemia, upward displacement of the diaphragm, or hydrothorax, or from all three of these conditions.

Among the objective phenomena, the most obvious is the splenic tumor, which may extend well below the navel and even to the symphysis. The notches on the anterior margin of the organ are often palpable, and sometimes a sense of crepitation, due to adhesions, may be elicited. Subjective sensations may be wanting, but many patients complain of a feeling of weight in the abdomen and not rarely localized pain and tenderness exist as a result of peritonitic adhesions. A decrease in the volume of the spleen may occur under treatment, or after hemorrhage or diarrhea.

*The Blood.*—The changes in the blood are of the first importance and alone are distinctive. The most striking feature is the great increase in the number of leucocytes, the count usually varying between 100,000 and 500,000, but occasionally exceeding 1,000,000. It is noteworthy, however, that during spontaneous remissions, during treatment with x-rays or benzol, and after an intercurrent infection the count may be normal. Although all varieties of white cells are, as a rule, in excess, special importance attaches to the large number of myelocytes, cells which normally do not enter the blood, but which in myeloid leukemia constitute from 10 to 50 per cent. of the total number of leucocytes—a very much larger proportion than is observed in any other condition. The neutrophilic myelocytes are much more abundant than the eosinophilic, although the latter may be numerous. In the later stages of the disease myeloblasts[1] may replace to a variable extent the myelocytes. The total number and, as a rule, the percentage of both eosinophiles and basophiles are increased. Although always relatively decreased, the polymorphonuclear neutrophiles and lymphocytes may be absolutely increased. The red corpuscles may not be reduced in number until a later period of the disease and then there is usually marked oligocythemia (2,000,000 or less), with the presence of many nucleated forms, especially normoblasts. Indeed, in rare instances a slight polycythemia is observed at an early period. Even when the red-cell count is approximately normal evidence of disturbed erythropoiesis is often shown by a distinct variation in the size and shape of the red corpuscles. Occasionally, too, polychromatophilia, fine stippling, and a few normoblasts may be observed. As a rule, the number of platelets is increased. The color-index is usually low. Charcot-Leyden crystals are sometimes found in blood-films that have been allowed to dry.

The composition of the urine is not characteristically altered, but a number of authors have reported increased elimination of uric acid and purin bases. The basal metabolism is usually considerably increased and in some cases exceeds that of severe hyperthyroidism.

**Complications.**—Thrombosis of the peripheral veins is not uncommon. Hemorrhages into the brain sometimes occur and may be the cause of death. Reports of tuberculosis as a complication have been somewhat frequent. Gangrenous processes occasionally appear, as in lymphoid leukemia. Ulceration of the intestines has been noted by a number of writers. Leukemic polyneuritis has been described.

[1] Myeloblasts are immature myelocytes with a reticulated nucleus, with an absence of granules or a few azure granules, and usually with a positive oxidase reaction. Many hematologists favor the view that they are mother cells and are the precursors of both nucleated red cells and the granular leucocytes.

**Diagnosis.**—The diagnosis of myeloid leukemia is often suggested by enlargement of the spleen and anemia, but as a number of other conditions, such as chronic malaria, kala-azar, splenic anemia, amyloid spleen, malignant growths of the spleen, and some cases of pernicious anemia, also produce both of these symptoms, and moreover as both splenic enlargement and anemia are occasionally absent in myeloid leukemia, it is evident that the blood-picture is the only criterion. A high percentage of myelocytes is sufficient to establish the diagnosis, even if the total number of leucocytes is not increased, as may be the case during remissions.

**Prognosis.**—Chronic myeloid leukemia is incurable, but remissions are not uncommon and temporary improvement often occurs under appropriate treatment. Five or six years, however, may be taken as the maximum duration of life. Death may result from exhaustion, hemorrhage, or an intercurrent infection, such as tuberculosis, pneumonia or pyococcic infection.

**Treatment.**—An effort should be made to maintain the general nutrition by regulating the diet and attending to hygienic measures. Rest is helpful. Among drugs, chemically pure benzol often produces marked temporary improvement, although it is not free from dangerous toxic properties, and it not rarely produces unpleasant symptoms, such as nausea and vomiting, headache and dizziness. It is best given in capsules with equal amounts of olive oil, the dose being cautiously increased from 10 minims (0.6 mil) to 20 minims (1.2 mils), three times a day. During the treatment the patient should be at rest, preferably in a hospital, and blood-counts should be made at frequent intervals. When the leucocytes have been reduced to 25,000 per cubic millimeter the administration of the benzol should be immediately suspended. Persistent headache, evidences of renal irritation, increasing anemia or even a very rapid fall in the leucocyte count should also be the signal for withdrawal of the drug. Pushed too far, the use of benzol may result in total atrophy of the hemogenetic tissue. Arsenic in doses gradually increased to the point of toleration is also of service, especially when the red-cells and hemoglobin are diminishing. If the stomach is intolerant intramuscular injections of sodium cacodylate, in doses of 2 grains (0.13 gm.) every other day, may be substituted for arsenic by the mouth. Of all therapeutic agents, however, the roentgen ray is the most generally useful. Skillfully applied, with its effects controlled by repeated blood examinations, it may suppress all symptoms of the disease for months, although it never alters the final result. According to Stengel and Pancoast the best results are achieved when the ray is applied to the bones, various portions of the body being treated in succession, and the spleen not exposed until it is reduced considerably in size and the patient's general condition is much improved, and even then only with caution. Radium and thorium-x, which also possesses radioactive properties, sometimes succeed in cases which prove refractory to the x-ray. Radiotherapy may often be combined advantageously with the benzol treatment. Splenectomy is rarely advisable, although Giffin of the Mayo Clinic[1] reports encouraging results in at least 6 of 26 cases in which operation was performed after the blood-picture was brought to normal by the use of radium, x-ray, or benzol.

## CHRONIC LYMPHOID LEUKEMIA

**Morbid Anatomy.**—The most conspicuous alterations are usually found in the *lymph-nodes*, which are enlarged, soft and of a grayish-white or reddish-white color. Any or all of the lymph-nodes may be affected, the localiza-

[1] Minnesota Med., 1921, 12, 132.

tion and distribution of the process conforming to no known rule. The nodes in the cervical, axillary and inguinal regions are most often enlarged, but those of the chest, abdomen, and throat are involved in many cases. Microscopically, the whole internal structure of the nodes appears to be transformed into a uniform mass of lymphocytes. The *spleen* is usually enlarged, although rarely to the extent observed in chronic myeloid leukemia. Upon microscopic examination the venules and interspaces are found crowded with lymphocytes. In the *liver*, which is, as a rule, only slightly enlarged, there may be numerous isolated nodules of lymphoid tissue or a more or less diffuse infiltration of lymphocytes. In the *bones* the fatty marrow is largely replaced by firm grayish-red tissue, composed almost entirely of lymphocytes. Nodules of lymphocytic tissue, macroscopic or microscopic, are also found in many other localities, as in the kidneys, lungs, brain, organs of special sense, mucous membranes, serous membranes and skin.

Although definite knowledge concerning the nature of the process is still wanting, the essential feature is apparently an extensive overproduction of lymphocytes from lymphoid tissue wherever it occurs, with a ready discharge of the new cells into the blood stream. The circumscribed lymphocytic nodules found throughout the body are probably the result of a proliferation of lymphoid tissue normally present, although, the possibility of metastasis or transplantation of cells from the lymph-nodes, bone-marrow, etc., cannot be altogether excluded.

**Symptoms.**—The onset is insidious and in the majority of cases the patient is first made aware of his disease by enlargement of the lymph-nodes or a gradual loss of weight and strength. The enlargement of the lymph-nodes, which is often slight, may be more or less general or limited to several groups or even a single group of nodes. The neck, axillæ and groins are the favorite sites, but other nodes, such as the thoracic, retroperitoneal and mesenteric, and the tonsils may also become enlarged. The affected nodes rarely fuse with one another, are not sensitive to pressure, and show little or no tendency to become adherent to the skin or to suppurate. Occasionally, there are no external lymphomas, but postmortem, large nodular masses are found in the thorax or abdomen. The spleen is usually enlarged, but, as a rule, much less so than in myeloid leukemia.

A slight increase in the size of the liver may also be noted. Evidences of anemia, such as pallor, weakness, palpitation, dizziness, edema, etc., usually appear somewhat early. Digestive disturbances are not so pronounced as in myeloid leukemia, and hemorrhages are uncommon. Febrile attacks occur from time to time. Cough, due to enlargement of the bronchial lymph-nodes, may be a troublesome symptom, and toward the end of the disease dyspnea, due to anemia, to leukemic infiltration of the lungs, or more rarely, to bronchial stenosis, is often a conspicuous feature. Leukemic infiltration or hemorrhage in the labyrinth of the ear may cause deafness, in the fundus of the eye, impairment of vision, and in the orbit, exophthalmos. Changes in the skin are occasionally observed, the lesions presented usually consisting of pale or reddish nodules of various size and shape, or of infiltrated, eczematoid plaques, scattered over the body and associated, as a rule, with intense itching. Exceptionally, pruritus alone occurs.

*The Blood.*—The blood alterations are characteristic. The number of leucocytes is greatly increased, although usually much less so than in myeloid leukemia, the count not often exceeding 100,000 and sometimes being as low as 30,000. The increase consists exclusively of lymphocytes, chiefly small ones, the relative proportion of these cells to the other varieties usually being 90 or 95, or higher. With the occurrence of anemia the red cells

undergo the same changes as are observed in myeloid leukemia, but nucleated forms are, as a rule, less abundant.

**Prognosis.**—The disease is always fatal and lasts from 6 months to 3 or 4 years. Its course is not infrequently marked by remissions and exacerbations. Death results from acute exacerbation, from intercurrent infection, or from the cachectic process itself.

**Diagnosis.**—The diagnosis is seldom difficult, if the blood is carefully examined. Lymphocytosis accompanying *streptococcic adenitis* may be distinguished by the recognition of an infectious origin for the adenitis, by the much lower percentage of lymphocytes in the differential count, and by the course of the disease. The lymphocytosis of *whooping cough* should be readily excluded. In *tuberculous adenitis* high leucocyte counts are uncommon, and, moreover, the affected nodes are likely to be tender, to fuse with one another, to become adherent to the skin or fixed to adjacent structures, and to soften and suppurate. *Hodgkin's disease*, which also produces painless and progressive enlargement of various groups of lymph-nodes, may usually be differentiated by the absence of leukemic changes in the blood, although it must be borne in mind that leukemia at a very early period and in remissions may be aleukemic. To establish the diagnosis with certainty it is sometimes necessary to excise one of the superficial nodes and to make a careful histologic study of it.

**Treatment.**—The treatment of chronic lymphoid leukemia is virtually that of chronic myeloid leukemia, although, as a rule, the former will be found to be less susceptible both to benzol therapy and to radiation with the roentgen ray than the latter.

## ACUTE LEUKEMIA

Acute leukemia is comparatively rare, but in children it is the prevailing type of leukemia. It has many features suggesting that it is an acute infectious process and a disease distinct from chronic leukemia, but thus far no organism has been demonstrated as an etiologic factor. According to the type of the leucocyte that floods the tissues and the circulating blood, two forms are recognized, the *lymphoid* and the *myeloid*, although many writers believe that the primary change in both forms is in the bone-marrow and that the lymphatic structures are involved secondarily. The bone-marrow is gray or reddish-gray and extremely cellular, the predominant cells being mature or immature lymphoid cells (lymphoblasts) in one group of cases and myeloid cells, especially immature forms (myeloblasts), in another group.

**Symptoms.**—In many cases the onset is abrupt with pseudomembranous, ulcerative or gangrenous inflammation of the mouth, gums or tonsils, the condition in consequence often being ascribed to diphtheria or to streptococcic infection. In other cases local hemorrhages, for example from the nose or kidneys, is the first conspicuous feature. Somewhat less frequently, perhaps, the onset is gradual, lassitude, weakness, vague pains, and more or less anemia preceding by several weeks or months the more characteristic symptoms. In a fourth group of cases localized enlargement of the lymph-nodes, especially the cervical, is the first symptom to attract attention. Whatever the mode of onset, the clinical picture of the fully developed disease resembles that of an acute infection, pallor, loss of flesh and strength, irregular fever, and hemorrhages from the mucous membranes and into the skin, retina, viscera, etc., being the most constant symptoms. Enlargement of the lymph-nodes, tonsils, and spleen, usually moderate, is commonly present, but is not inevitable. Convulsions sometimes occur at the onset,

and occasionally symptoms closely simulating those of meningitis supervene as a result of hemorrhage or leukemic infiltration beneath the meninges. Paralysis of peripheral cranial nerves in consequence of bleeding into their substance has also been observed.

*The Blood.*—The leucocyte count is, as a rule, high—50,000 to 200,000, or more, although in some instances it is only slightly above the normal. In the lymphoid form the prevailing cell in one group of cases (20 per cent.) is the small lymphocyte and in another group it is a large mononuclear cell with homogeneous basophilic cytoplasm. The latter is probably not the normal large lymphocyte, as it is sometimes thought to be, but the forerunner of it, or a lymphoblast. In the myeloid form the excess of leucocytes is made up largely of non-granular myeloblasts, although cells representing transitional stages between non-granular myeloblasts and granular myelocytes may also be found. Myeloblasts closely resemble the large mononuclear forms (lymphoblasts) of lymphoid leukemia, but can usually be distinguished by the oxidase reaction.[1] The more acute the disease the greater is the proportion of myeloblasts over myelocytes (Naegeli).[2]

In the majority of cases, but not in all, there is a very rapid decrease in the number of red cells, the count sometimes falling to 1,000,000, or less. The color-index is often high, and not rarely there are, as in pernicious anemia, many nucleated red cells, both normoblasts and megaloblasts, with poikilocytosis and polychromasia. Acute leukemia terminates fatally in from a few days to a few months, the average duration being about 6 weeks. The diagnosis can rarely be made without a blood examination. Many of the cases have probably been mistaken for diphtheria, scurvy, purpura hemorrhagica, glandular fever, or septic infection. There is no known effective treatment. Injections of normal horse serum and transfusion of blood have been tried, but without favorable results. The use of the roentgen ray is contraindicated.

## ATYPICAL LEUKEMIA

**Aleukemic Leukemia.**—Cases of leukemia are occasionally observed in which the white-cell count is only slightly increased or is normal or even subnormal and there is an absolute and often a relative increase of certain forms of mature or immature leucocytes. Transitions from the leukemic to this aleukemic type or vice versa may occur. The cases have been classified *aleukemic myelosis* or *aleukemic lymphadenosis* according as the myeloid cells or the lymphoid cells predominate. Occasionally aleukemic leukemia is characterized by the presence in the blood of a large number of cells resembling normal large mononuclear or transitional forms (*monocystic leukemia*). The course of aleukemic leukemia may be acute or chronic.

**Leukanemia.**—The term leukanemia was introduced by Leube[3] to describe a rapidly progressive disorder of the blood-forming tissues characterized by changes in the blood and also in the bone-marrow, spleen and lymph-nodes that suggest a combination of pernicious anemia and myeloid leukemia. The chief features are severe anemia, a high color-index, the presence of many nucleated red cells and of large mononuclear leucocytes in the peripheral blood, a tendency to hemorrhages, and enlargement of the spleen and liver.

[1] The cytoplasm of cells containing oxidases—myeloblasts and their derivatives (myelocytes and polymorphonuclears—stains blue with a solution consisting of equal parts of 1 per cent. aqueous solution of alphanaphthol and dimethylparphenylendiamin. Lymphocytes and red cells do not stain blue.

[2] Leukemia u. Pseudoleukemia, 1913.

[3] Sitzungsber. d. med. Ges., Wurzburg, 1900.

The whole number of leucocytes may or may not be increased, but there is always high percentage of large non-granular mononuclear white cells, which are apparently myeloblasts. The nature of leukanemia is obscure, but the condition appears to be due to the action of some noxious agent upon the entire hematogenic bone-marrow, with simultaneous derangement of both the erythroblastic and leukoblastic functions.

**Pseudoleukemia.**—Cohnheim originally applied the term pseudoleukemia to a condition clinically identical with lymphoid leukemia, but without the leukemic blood picture. Later the term was given a broader scope and applied to a variety of ill-defined lymphomatoses unaccompanied by any increase, relative or absolute, in the circulating leucocytes. In the light of our present knowledge, however, it is doubtful whether there is any pathologic entity that may properly be so designated. Complete studies, including careful histologic examinations, would probably show that cases of so-called pseudoleukemia are in reality examples of one of the following conditions: (1) leukemia in an early stage or in remission, (2) Hodgkin's disease, (3) generalized tuberculous lymphadenitis, or (4) lymphosarcoma with restriction of the metastases to the lymphoid tissues. Certainly, if the term pseudoleukemia is used at all it should be reserved for cases which are the exact counterpart of lymphoid leukemia, both as regards the generalized enlargement of the lymph-nodes and also the histological changes in the lymph-nodes, but in which the leukemic blood picture is absent throughout.

**Leukosarcoma.**—This term, introduced by Sternberg, is used to designate a rare disease of the hematopoietic system characterized by the occurrence in some organ or tissue of an infiltrating tumor-like mass, the cells of which are lymphoid or myeloid and apparently escape into the blood in great numbers, producing the leukemic blood-picture and causing wide-spread metastases. Although the process is apparently neoplastic (sarcomatous), it differs only in degree from those more aggressive forms of leukemia in which small tumor-like growths appear in the skin and elsewhere.

Leukosarcoma occurs especially in children, although adults are sometimes affected. It is much more frequent in males than in females. The most striking form of the disease is that known as *chloroma*, because of the green color of the tumor-like mass. The nature of the green color has not been definitely determined, but it is supposed to be due to greenish refractive lipoid granules. Histologically, two types of chloroma may be distinguished, one composed of lymphoid cells, the other of myeloid cells. The favorite site is the orbital region of the skull, but the process may begin in the vertebræ, the sternum, a long bone or even one of the viscera. Enlargement of the lymph-nodes in various parts of the body and of the spleen, changes in the bone-marrow, and secondary deposits in almost every organ and tissue are common findings. Painful exophthalmos, with impairment of vision and disturbances of hearing, is often the first clinical indication. The other features are those of acute or subacute leukemia, and include general weakness, progressive anemia, hemorrhagic or purpuric manifestations, and an overflooding of the blood with monuclear leucocytes, of either the lymphoid or myeloid type. Non-chloromatous leukosarcoma may have its primary site in the thymus, intestine, tonsil or elsewhere. In its essential pathology and clinical course it does not differ from the chloromatous form.

Leukosarcoma is not appreciably influenced by any known treatment and terminates fatally from a few weeks to several months.

## LYMPHOSARCOMA

This condition, first described by Kundrat[1] in 1893, is a malignant tumor formation arising in a group of lymph-nodes or in the lymphoid tissue of a mucous membrane, and spreading thence by way of the lymphatics to adjacent lymph-nodes and infiltrating the surrounding tissues. Although its extensions are often widespread, the process usually remains regional, distant metastases by way of the blood stream being exceptional. The spleen and bone-marrow are rarely involved. Histologically, the tumor consists of atypical reticular tissue in the meshes of which are lymphoid cells of variable size.

The common sites of lymphosarcoma are the neck, with the starting point in the cervical nodes or the mucosa of the tonsillar ring, the mediastinum, the retroperitoneal region, and the intestine. Clinically, the tumor forms a bulky uneven mass, often reaching large proportions and resulting in necrosis and ulceration. Extension in the cervical form may be upward to the skull or downward to the thorax; in the mediastinal form, to the pleura, pericardium and lung; in the retroperitoneal form to the peritoneum, intestine and liver. Intestinal lymphosarcoma may be diffuse or in the form of nodular masses projecting at various points into the lumen of the bowel. Ulceration is common and stenosis of the intestine, perforation, or chronic peritonitis with chylous effusion may occur. In all forms of the disease anemia and cachexia appear early. Fever is also common. The blood-picture is not characteristically altered. In the early stages there may be only a moderate excess of the polymorphonuclear leucocytes, but late in the disease there is often an overwhelming preponderance of lymphocytes. The affection is invariably fatal and usually lasts from 4 to 6 months. In the intestinal form the duration may be only a few weeks. The diagnosis is sometimes difficult. Lymphosarcoma is distinguished from *adenitis* by its local destructive capacity and its tendency to form true metastases. In *lymphoid leukemia* there are usually multiple lymphomas with little destructive tendency and the blood throughout shows pronounced lymphocytosis. In *Hodgkin's disease* the lymphatic lesions are, as a rule, generalized, and locally are less destructive and aggressive, and the histologic picture is characteristic. The resemblance to *leukosarcoma* may be very close. Indeed, distinctions cannot always be sharply drawn between leukemia on the one hand and lymphosarcoma and leukosarcoma on the other. Webster[2] from a careful study of 123 cases concludes that lymphosarcoma, lymphatic leukemia and leukosarcoma are probably different expressions of the same disease; that leukosarcoma combines the features of lymphosarcoma and lymphatic leukemia, and that a localized lymphosarcoma may under certain conditions become generalized and, with a blood picture of lymphatic leukemia, may terminate as leukosarcoma.

**Treatment** by excision, the use of x-ray and the administration of arsenic is sometimes beneficial, but never curative.

## GRANULOMA FUNGOIDES

Granuloma fungoides, or mycosis fungoides, is a comparatively rare disease characterized for months or years by a more or less diffuse eczematoid eruption, usually with itching; and later by the appearance of infiltrated patches or nodules in the skin, which tend to ulcerate and form fungoidal

[1] Wien. klin. Woch., 1893, vi, 211.
[2] Johns Hopkins Hosp. Bull., 1920, xxxi, No. 38.

or mush room-like growths; by enlargement of the lymph-nodes; and, not infrequently, by flooding of the blood with lymphoid cells, the picture finally resembling that of acute leukemia. The disease appears to be related on the one hand to Sternberg's leukosarcoma and on the other to lymphosarcoma. Ten of Sequiera's[1] 13 cases were in males. X-ray treatment has sometimes produced a symptomatic cure. Internally, arsenic has occasionally proved useful.

## HODGKIN'S DISEASE

### (Lymphogranulomatosis)

**Definition.**—An infectious granulomatous disease, for the most part chronic, characterized by enlargement of the lymph-nodes, progressive anemia of the secondary type with little or no increase of the leucocytes, and a fatal termination.

Hodgkin[2] described the disease in 1832, but he grouped with it a number of other lymphomatous conditions of an entirely different nature.

**Etiology.**—Hodgkin's disease is more frequent in males than in females, and although it may occur at any age, it is especially common in young adults. The process is undoubtedly infectious, but the specific organism which produces it has hitherto escaped detection. The view originally expressed by Sternberg (1898) and more recently endorsed by Türk,[3] by Fraenkel and Much,[4] Steiger[5] and others that it is of tuberculous origin has been rejected by the majority of writers, although it is generally admitted that Hodgkin's disease bears a close resemblance to certain forms of tuberculous lymphadenitis, even in the histological picture, and that the association of tuberculous lesions with Hodgkin's disease is frequently observed. Those who are opposed to Sternberg's theory ascribe the occurrence of tuberculous processes in certain granulomatous nodes to an associated or superimposed infection unrelated to Hodgkin's disease. Recently Bunting and Yates,[6] Billings and Rosenow,[7] Torrey[8] and others have reported the isolation of a diphtheroid bacillus from Hodgkin's lymph-nodes, but the evidence in favor of its being the specific cause of the disease is not convincing. Diphtheroid organisms have been found in many other conditions and even in normal lymph-nodes (Bloomfield), and the results of inoculation studies are by no means in accord.

**Morbid Anatomy.**—The changes in the lymph-nodes are apparently of an inflammatory nature and distinct from the lymphoid or myeloid hyperplasia of leukemia. The affected nodes are round or oval, discrete or loosely jointed in groups, and soft or hard, according to the degree of fibrosis present. Occasionally, however, adjacent nodes fuse and the granulomatous formation extends through the capsules to surrounding tissues. The walls of the blood-vessels are not rarely invaded. While the size of the lymphomatous masses varies, it is, as a rule, considerably larger than that seen in lymphoid leukemia. On section, the nodes may be grayish or pinkish gray and

[1] Brit. Jour. Derm., 1914.
[2] Medico-Chirurg. Trans., 1832.
[3] Wien. klin. Woch., 1903, xvi, 1073.
[4] Ztschr. f. Hyg., 1910, lxvii, 159.
[5] Ztschr. f. klin. Med., 1914, lxxix, 452.
[6] Jour. Amer. Med. Assoc., 1913, lxi, 1803; *ibid.*, 1914, lxii, 516.
[7] Jour. Amer. Med. Assoc., 1913, lxi, 2122.
[8] Jour. Med. Research, 1916, xxxiv, 65.

semitranslucent or yellow and opaque. In typical cases the histological picture, as shown by the studies of Sternberg, Dorothy Reed,[1] MacCallum,[2] Longcope[3] and others, is characteristic. At the beginning of the process there is merely a proliferation of the lymphoid cells, but soon the follicles and sinuses are obliterated and the whole structure of the node becomes a network of overgrown connective tissue, the meshes of which are filled with lymphoid cells, endothelioid cells, mononuclear and multinuclear giant cells, and perhaps, eosinophiles and plasma cells, in varying proportions. The endothelial cells are large pale cells, rich in cytoplasm and with an elongated, vesicular, faintly-staining nucleus. The giant cells, which are especially characteristic, are four or five times the size of the ordinary lymphoid cells. Many of them have several vesicular nuclei, which are indented or lobed, and in which nucleoli can be made out with great regularity. Evidences of necrosis are not often seen. In the later stages, however, the connective tissue proliferation becomes marked, and ultimately the whole node may be transformed into a fibrous mass, with only a few scattered areas of characteristic tissue. Besides the cases with a characteristic histological picture, there are others, apparently no less typical, in which the nodes show only a proliferation of the reticulum and simple lymphoid hyperplasia.

Gray nodules of granulomatous tissue, with its peculiar large cells, may also be found in the spleen, which is often considerably enlarged, in the liver, gastrointestinal tract, lungs, serous membranes, bone marrow, etc. Such nodules are probably not true metastases, but preëxisting foci of lymphoid tissue undergoing the granulomatous change.

**Symptoms.**—In the majority of cases the first symptom is painless enlargement of a group of lymph-nodes, usually those in the neck being primarily affected, although in some instances the axillary, inguinal, thoracic or abdominal nodes are the first to swell. Wherever the primary focus, generalization occurs sooner or later, the disease only rarely remaining localized in one set of nodes. The lymphomatous tumors, which sometimes attain an enormous size, may be hard or soft. The individual nodes comprising them are, as a rule, distinctly palpable, although eventually they may fuse with one another and become adherent to the overlying skin and adjacent tissues. A splenic tumor develops in about two-thirds of the cases and may reach large proportions. The liver is enlarged somewhat less frequently. Local symptoms resulting from the compression of important structures by the enlarged nodes are not infrequent; thus there may be edema of the face or other regions, dyspnea and cough, pains in the abdomen or limbs, various gastrointestinal disturbances, effusions into the serous sacs, or icterus.

For a variable period of weeks, months or years there is usually little or no constitutional disturbance, but with the generalization of the disease, malaise, anemia and cachexia appear. Fever, frequently accompanied by sweats and chills, also occurs at some time in virtually every case. It may be of the recurrent type, continuous with daily remissions, or intermittent. Cutaneous symptoms precede, accompany or follow the other manifestations of the disease in from 15 per cent. (Westphal[4]) to 25 per cent. (Ziegler[5]) of all cases, the most common being persistent pruritus, a papular prurigo-like exanthem, urticaria, edematous swellings, bronze-like pigmentation and petechiæ.

In the early stages the blood shows no changes, but as the disease pro-

[1] Johns Hopkins Hosp. Reports, 1902, x, 133.
[2] Tr. Assoc. Am. Phys., 1902, xii, 350.
[3] Bull. Ayer Clin. Laboratory, 1903–4.
[4] Quoted by Bunting and Yates: Bull. Johns Hopkins Hosp., April, 1917.
[5] Ziegler, Kurt: Die Hodgkinsche Krankheit, Jena, 1911.

gresses anemia of the secondary type develops and may become profound, the red cells sometimes falling to 2,000,000 or less and the hemoglobin to 40 or even 30 per cent. The leucocytes are not characteristically affected. The number may be about normal, decreased, or slightly in excess, the latter especially during exacerbations. The lymphocytes are often relatively or absolutely increased and in some cases there is a pronounced eosinophilia. A leukemic transformation of Hodgkin's disease has never been observed.

**Exceptional Forms.**—A so-called *larval form* is occasionally met with, in which there is no enlargement of the palpable lymph-nodes, but with the chief lesions in the mesenteric or retroperitoneal nodes. In this form fever and gastrointestinal disturbances are very common, the condition sometimes closely simulating typhoid fever. In other cases (*mediastinal form*) the thoracic nodes, while not exclusively affected, bear the brunt of the infection and in consequence symptoms due to compression of the trachea, bronchi, large vessels, etc., become a conspicuous feature. A *gastrointestinal form* has been described by several writers. In some of the cases the lesions were distinctly granulomatous and free from tubercle bacilli, but in others they seem to have been more closely allied to lymphosarcoma. A few cases of Hodgkin's disease originating in the spleen have been reported (*primary splenic form*).

**Diagnosis.**—Although Hodgkin's disease may usually be suspected by the occurrence of a painless progressive enlargement of the lymph-nodes without leukemic changes in the blood, the diagnosis can only be made definitely by the microscopic examination of an excised node. It cannot be differentiated clinically from certain cases of tuberculous lymph-adenitis, lymphosarcoma, leukemia in an aleukemic stage, and even simple hyperplastic lymph-adenitis. Even the histological picture is occasionally equivocal, suggesting on the one hand Hodgkin's disease and on the other lymphosarcoma or tuberculosis. *Sarcomas of the lymph-nodes, both the ordinary forms (round-cell, spindle-cell, etc.) and lymphosarcoma* may sometimes be distinguished clinically by their rapid growth, local destructive properties, often resulting in necrosis and ulceration, tendency to form true metastases in distant organs, and the early development of cachexia. *Ordinary regional tuberculous lymphadenitis* may usually be differentiated by the tendency of the enlarged nodes to fuse, to become adherent to overlying tissues, and to break down and form sinuses, as well as by a reaction to tuberculin tests. In doubtful cases, definite enlargement of the spleen and marked pruritus point rather to Hodgkin's disease than to either sarcoma or tuberculosis. Finally it must be remembered that tuberculous infection may sometimes be demonstrated in the lesions of true Hodgkin's disease, and also that Hodgkin's granulomas occasionally undergo sarcomatous transformation (Yamasaki, Karsner, Ewing).

**Prognosis and Course.**—The disease is invariably fatal. The duration varies from a few weeks in acute cases (rare) to many years, but is usually about two years. Remissions with temporary regression of the enlarged lymph-nodes are sometimes observed. Death may be due to cachexia, an intercurrent infection, particularly tuberculosis, or, rarely, pressure on some important structure. Paraplegia from pressure upon the spinal cord has been noted at least twice (Osler, Davis[1]).

**Treatment.**—Treatment by x-rays or radium emanations, directed not only to the palpable lymph-nodes, but to all the lymphoid structures of the body, including the mediastinal and abdominal nodes, often produces marked improvement, but is never curative. Yates and Bunting[2] recommend as a

[1] Bull. of Lying-In Hosp. of City New York, Mar., 1911.

[2] Jour. Amer. Med. Assoc., 1917, lxviii, 747.

preliminary measure the elimination of all possible foci of infection, such as may exist in the tonsils, teeth, etc., and, after this has been accomplished, the complete extirpation of all affected lymphoid tissue accessible to the knife, with postoperative radiation and the use of an immune serum prepared with the diphtheroid organism often found in the lesions. With this plan of treatment, they believe that a cure may be obtained in about 20 per cent. of all cases. Other writers of large experience, however, are not so optimistic about operative measures, although they do not deny the possibility that complete excision, if undertaken when the process is confined to a single focus, and followed by radiotherapy, may occasionally prove curative. As to drugs, arsenic in the form of Fowler's solution by the mouth or of arsphenamin by intravenous injection, is sometimes of definite value, but it is without specific or lasting effect. The hygienic and dietetic treatment of the disease is that of simple anemia.

## MULTIPLE MYELOMA

Multiple myeloma is a malignant tumor of the bone-marrow, affecting simultaneously a number of bones, accompanied in many instances by Bence-Jones proteinuria, terminating fatally in from a few months to several years, and only rarely causing metastases in the organs.

The disease, which is comparatively rare, appears most frequently in middle life and occurs chiefly in men. The ribs, sternum, skull, vertebræ and pelvis are favorite sites. The process may occur as a diffuse infiltration of the marrow, but much more frequently it forms multiple circumscribed tumors. In the majority of cases the cells of the tumors are plasma cells, round or oval, with single or multiple eccentric nuclei, and non-granular cytoplasm. In some cases, however, the cells correspond more closely to lymphocytes, and in others, to myelocytes or myeloblasts. The usual *symptoms* are continuous or paroxysmal pains in the bones, anemia, emaciation, Bence-Jones proteinuria (see p. 740), and, in the later stages, marked skeletal deformities and fractures. The blood changes are usually those of secondary anemia. In a few instances an excess of myelocytes has been observed in the blood and in at least two cases (Aschoff, Beck) plasma cells were found in it. Metastases in the organs are exceptional, but may occur (Pepper and Pearce[1]). X-ray examination sometimes aids in the diagnosis. Proteinuria is not present in every case and occasionally it is observed in other conditions, particularly carcinoma of bone and leukemia.

## ANEMIA

The term anemia is used to designate a diminution in the total volume of blood, or a deficiency of erythrocytes or of hemoglobin, or of both of these constituents. Changes in the plasma, although little understood and less conspicuous than changes in the other elements, are in reality of primary importance in many cases. A satisfactory classification of the various anemias is not possible at present, because our knowledge of their etiology is far from complete. The terms *primary* and *secondary* anemia, however, are still used, the former being applied to anemias the causes of which are wholly

[1] Jour. Med. Research, 1917, xxxvii, No. 1.

unknown, and the latter to anemias which are symptomatic of well understood pathological conditions. This division, while useful for clinical purposes, must not be regarded as final, for strictly speaking there can be no such thing, of course, as a primary anemia. In the last analysis the anemic state is the result of one of three causes: (1) a loss of blood from hemorrhage, (2) increased blood destruction, or (3) decreased blood formation. Therefore the following grouping, based on one proposed by Morawitz, although open to criticism, seems to be logical:

I. Anemias due to loss of blood through hemorrhage:
   (*a*) Acute posthemorrhagic.
   (*b*) Chronic posthemorrhagic.
II. Anemias due to increased blood destruction (hemolytic anemias):
   (*a*) Due to certain known chemical poisons (nitro-benzol, phenylhydrazin, potassium chlorate, etc.).
   (*b*) Due to poisons of certain intestinal parasites, especially Dibothriocephalus latus.
   (*c*) Due to microörganismal toxins (malaria, septicemia, syphilis, etc.).
   (*d*) Due to unknown hemolysins:
      1. Pernicious anemia (Addison-Biermer type).
      2. Anemia of pregnancy.
      3. Splenic anemia.
      4. Anemia accompanying congenital hemolytic icterus.
III. Anemias due to deficient blood building:
   1. Myelopathic: Due to encroachment upon the bone-marrow by tumors, overgrown leukoplastic tissue (leukemia), osteosclerosis, etc.
   2. Hypoplastic, for example:
      (*a*) In wasting diseases, inanition, etc.
      (*b*) Aplastic or aregenerative anemia (cause often unknown).
IV. Chlorosis.
V. Von Jaksch's Disease.

**Posthemorrhagic anemia** may be acute or chronic, according to the amount of blood lost and the rapidity with which the bleeding occurs. The acute form is observed after mechanical injuries in which large bloodvessels are opened, in pulmonary tuberculosis with erosion of a branch of the pulmonary artery, in cirrhosis of the liver with rupture of esophageal varices, in some cases of gastric or duodenal ulcer, in ectopic pregnancy with rupture of the Fallopian tube, etc. The quantity of blood that may be lost without causing death varies greatly in different persons. According to Hayem recovery is possible, as a general rule, if the total volume of blood lost does not exceed $\frac{1}{18}$ (5.5 per cent.) of the individual's body weight.

Chronic posthemorrhagic anemia is the result of small and repeated losses of blood, such as may occur from peptic ulcer, hemorrhoids, uterine fibromata, hemophilia, etc. The anemia varies in intensity, but it may be very profound and, so far as the blood changes are concerned, even indistinguishable from pernicious anemia.

The **anemias due to increased blood destruction** form a very large group of cases. The hemolytic agent may be an ordinary chemical poison the nature of which is definitely known, or it may be a toxin of microörganismal origin. Certain bacteria, for example, the hemolytic streptococci, produce powerful blood-destroying poisons and may bring about extreme grades of anemia in a comparatively short time. In some of the chronic infections several factors may operate to produce anemia. The anemia of malaria, for instance, is probably due largely to hemolysis produced by the plasmodia, although mechanical destruction of the corpuscles by the parasites within them is undoubtedly also a factor. In the anemia of chronic pulmonary tuberculosis losses of blood (hemoptysis), hemolysis by products of the invading organisms, and deficient hemogenesis as a result of inanition may all play a part. Dibothriocephalus latus anemia is essentially a hemolytic

anemia. It is not due to losses of blood, but apparently to a poison secreted by the living worm or liberated from segments of the dead parasite. The anemia rarely occurring in pregnancy, which may be of extreme grade, is thought to be the result of a hemolytic agent having its origin in the placenta. In certain cases of severe anemia, although there are definite evidences of excessive hemolysis, the nature and source of the poison still elude detection. The most conspicuous example of this group of cases is so-called pernicious anemia. The cause of the anemia accompanying hemolytic icterus also remains to be determined, although increased fragility of the red cells is present in many cases. It is doubtful whether splenic anemia is actually a disease entity. In many cases it appears to be a manifestation of visceral syphilis. In view of the effect of its removal, however, the spleen must be regarded as intimately associated with the cause of the anemia.

Hemoglobin set free in the plasma as a result of hemolysis is usually rapidly removed by the liver and spleen. If the hemolysis is excessive it may be made manifest by a subicteric tint of the skin, high values for urobilin and urobilinogen in the duodenal contents, urobilinuria, hemosiderosis, etc. Occasionally the destruction of blood cells occurs so rapidly and is so extreme that the liver and spleen are unable to take care of the free hemoglobin and in this case hemoglobinuria ensues.

**Anemia due to deficient blood building** is observed most frequently as a result of wasting diseases in which the bone-marrow shares with other organs in the general malnutrition. The term myelopathic anemia is applied to anemia caused by actual destruction or crowding out of the erythroblastic tissue of the bone-marrow, such as may occur in the later stages of leukemia from excessive overgrowth of leukoblastic tissue, in the rare cases of cancer in which metastatic nodules occupy the marrow-cavity of nearly every bone and in osteosclerosis with obliteration of the marrow-cavity in a large number of bones.

Apart from the aplastic stage into which hemolytic anemias sometimes pass when the regenerative power of the bone-marrow and other organs has become completely exhausted (secondary aplastic anemia), there appears to be a primary form of aplastic anemia arising from incapacity of the blood-forming organs alone, although many observers believe that aplastic anemia is never anything more than a severe hemolytic anemia, usually of the Addison-Biermer type, in which the same agency that caused the excessive hemolysis has also injured the bone marrow to such an extent that there is complete absence of regenerative response.

It is somewhat doubtful whether **chlorosis** should be classed among the anemias, as the peculiar blood changes of the disease, although of great importance, constitute only a part of its symptom-complex. The essential nature of the affection is not known, but the theory most in accord with the facts is that which ascribes the primary cause to a disturbance of the glands of internal secretion, especially the ovaries. As there is no evidence of excessive hemolysis in chlorosis, it may be assumed that the blood changes of the disease are due to deficient hematopoiesis.

Although **von Jaksch's**[1] **disease** (anemia pseudo-leukemica infantum) is included in the table of anemias there is some reason for believing that it is not a distinct clinical entity, but the expression of a number of conditions seriously affecting the blood, including splenic anemia, pernicious anemia and various forms of secondary anemia, the anomalous features being due to a difference in the reaction of the infantile hemopoietic organs to the causative factor. The condition is characterized by severe anemia, a low color-index,

[1] Wien. klin. Woch., 1889, ii.

persistent leucocytosis (20,000 to 50,000), pronounced enlargement of the spleen, in some cases slight enlargement of the liver and superficial lymph-nodes, and some tendency to spontaneous recovery. The disease occurs usually between the ages of six months and two years and is frequently associated with rachitis.

## SECONDARY ANEMIA

**Symptoms.**—The symptoms vary with the degree of the anemia. After a single copious hemorrhage they are largely the result of incomplete filling of the vessels and consist of pallor, shock, frequent yawning, nausea, fainting, etc. In less severe forms of anemia, without much reduction in the total volume of blood, such as may occur from repeated small hemorrhages, various infections and intoxications, carcinoma, starvation, etc., the general symptoms do not differ materially from those of pernicious anemia or chlorosis. Pallor of the skin and mucous membranes and muscular weakness are, as a rule, conspicuous features. The pulse is compressible and inclined to be frequent, and the extremities are usually cool. Dyspnea, especially on exertion, and palpitation are common causes of complaint. A soft systolic murmur may often be heard over the heart, and also a venous hum (*bruit de diable*), continuous during systole and diastole, at the root of the neck. There is a tendency to edema and to serous effusions, and sometimes hemorrhages occur beneath the skin and in the mucous membranes. The digestive functions are almost always disturbed. Referable to the nervous system, there are in many cases headache, vertigo, faintness, tinnitus, blurring of vision, and insomnia or somnolence. Amenorrhea or menorrhagia is not uncommon.

*Changes in the Blood.*—In acute posthemorrhagic anemia an examination of the blood immediately after the bleeding usually shows no reduction in the number of corpuscles or percentage of hemoglobin, since the blood as a whole is diminished in quantity and the plasma and cellular elements are proportionately involved in the loss. Very rapidly, however, the total volume of blood is restored by transference of fluid from the tissues and digestive tract, and a hydremic state supervenes. The cellular elements are replaced more gradually than the fluid and the regeneration of hemoglobin proceeds still more slowly than the erthropoiesis, and so for a time there is a disproportionate achromia. The rapidity with which the blood is restored to its normal condition depends upon the amount of blood lost, upon the general vigor of the patient, and upon the treatment that he receives. Usually after a hemorrhage involving a hemoglobin loss of 20 to 25 per cent., if the conditions are favorable, regeneration is effected in about 3 or 4 weeks.

During the regenerative period examination of the blood reveals oligocythemia, a low color-index, polychromatophilia, some variation in the size and shape of the red cells (anisocytosis), a few nucleated red cells, mostly normoblasts, a pronounced increase in the platelets, and a slight increase in the leucocytes, chiefly in the polymorphonuclear forms. With vital staining of the blood an increase in the percentage of reticulated red cells is also found.[1]

In the more chronic forms of secondary anemia examination of the blood reveals oligocythemia (4,000,000 to 2,000,000), more or less achromia, with a low color-index, slight or moderate poikilocytosis and anisocytosis, and an

[1] In vital staining the blood is stained before it has come in contact with air. The stain (brilliant cresyl blue) may be placed on the finger and the blood expressed into it. Normally, about 0.8 per cent. of the red cells are reticulated.

occasional nucleated red cell, usually of normal size. The percentage of reticulated red cells and the number of platelets are increased, as a result of the unusual activity of the hemopoietic organs. A slight or moderate polymorphonuclear leucocytosis is also present in many cases. In very severe forms of chronic secondary anemia the blood picture may approach that of pernicious anemia—marked oligocythemia, high color-index, embryonal types of cells (megalocytes, megaloblasts, etc.) leucopenia, blood-platelet diminution, etc.

**Treatment.**—In acute posthemorrhagic anemia the important indications are to raise the blood pressure in the medulla and to increase the volume of circulating fluid. The patient's head should be lowered and, if the loss of blood has been large, bandages should be firmly applied to all four extremities. To increase the bulk of the blood, water should be given freely and saline solution should be administered by proctoclysis, hypodermoclysis or intravenous infusion, or the transfusion of blood itself should be practised. In urgent cases, transfusion, direct or indirect, is of all measures the most effective. After the blood pressure has been restored and the acute symptoms have subsided the treatment is that of anemia from other causes.

In the treatment of chronic secondary anemia removal of the underlying cause is the chief indication. Other measures, although sometimes of service, are of secondary importance. The diet must be adapted to the digestive power of the patient. Generally speaking, it should be abundant, varied and nutritious. Meat, eggs, fat, green vegetables and milk are indicated. An abundance of fresh air, frequent bathing followed by vigorous friction of the skin, massage, an amount of physical exercise adjusted to the patient's strength and primary disease, and change of scene are all important aids in treatment. Of drugs, none is so generally useful as iron, which in many cases is best given in the form of Blaud's pill, 5 grains (0.3 gm.) after each meal for a week and then, if necessary, 10 grains (0.6 gm.) at the same intervals. Reduced iron and Basham's mixture are also reliable preparations. In cases with marked gastric disturbance citrate of iron may be given by intramuscular injection. Ampules containing 3 grains (0.2 gm.) of the drug in sterile solution are on the market and the contents of one of these may be injected every other day. Arsenic is often a useful adjuvant to iron. Fowler's solution may be chosen as the preparation and given in gradually increasing doses to the point of toleration. If arsenic is not well borne when given by the mouth it may be administered by intramuscular injection in the form of sodium cacodylate—½ grain (0.03 gram) daily, gradually increased to 2 grains( 0.13 gram ) daily.

In severe cases intravenous injections of arsphenamin are sometimes effective, even in the absence of syphilis. Reactions to the drug, however, must be avoided. In secondary anemia with a very low percentage of hemoglobin transfusion of blood may also result in marked improvement. Bitters, such as nux vomica and gentian, are frequently useful in combating anorexia arising from anemia. To secure the best results they should be given in liquid form about half an hour before meals.

## PERNICIOUS ANEMIA

(Addison-Biermer Anemia)

**Definition.**—A chronic disease of unknown etiology, often interrupted by remissions, but usually, if not invariably fatal, characterized by intense anemia with a marked tendency to the embryonal type of blood formation, and involving at least three factors, namely, increased hemolysis, stimula-

tion and finally exhaustion of the regenerative power of the bone-marrow, and an abnormality of splenic function.

The disease was accurately described by Addison[1] in 1855 and again by Biermer[2] in 1871, the latter employing for the first time the name "primary progressive pernicious anemia."

To be excluded from our conception of pernicious anemia of the Addison-Biermer type are a number of conditions closely resembling this disease, but having an obvious or, at least, a discoverable cause. In this group are the anemias due to certain known chemical poisons (nitrobenzol, phenylhydrazin, etc.), to invasion of the intestine by *Dibothriocephalus latus*, *ankylostoma duodenale*, *Balantidium coli* and other helminths, to certain chronic infections, such as syphilis, and to intoxications arising in the latter half of pregnancy.

**Etiology.**—The ultimate cause of pernicious anemia is still unknown. The disease is commonest in persons of middle age and is rare in childhood and youth. Males are somewhat more frequently affected than females. Social and hygienic conditions are without etiologic influence, and this is probably true also of heredity, although there are a few reported instances of multiple cases in one family (Cabot, Patek). William Hunter[3] has emphasized the importance of long-standing sepsis, oral and gastric, as a causative factor, but while most writers agree that infection of this origin may in some cases have a part in the process, the evidence is not convincing that it ever plays a preponderating rôle. Others ascribe the disease to some gastro-intestinal disturbance leading to injury of the mucosa and the absorption of hemolytic toxins of putrefactive origin or of undigested proteins which in the blood stream become transformed into hemolytic poisons. It has also been asserted that pernicous anemia is due to a disturbance of the lipoid mechanism of the body and the liberation of abnormal amounts of hemolytically active fatty acids. Whether anemia of the secondary type, such as that due to recurrent small hemorrhages, is ever a precursor of the true Addison-Biermer anemia is doubtful.

**Morbid Anatomy.**—In typical cases the skin has a lemon-yellow tint, the subcutaneous fat is fairly well preserved, and the muscles are unsually red. Petechiæ and effusions into the serous sacs are frequently found, the heart, liver, and kidneys are fatty, and the organs generally show considerable accumulation of iron-containing blood pigment. Inflammatory lesions are sometimes observed in the mouth, especially on the tongue, and in a large proportion of cases the mucosa of the stomach is smooth and atrophic.

The *bone-marrow*, especially that of the long bones, is dark red and unusually soft, the fatty portion being replaced by overgrown erythrogenetic tissue, which upon microscopic examination is found to be of an embryonal type. In it there are numerous groups of megaloblasts, intermingled with normoblasts, myelocytes, myeloblasts, and many large phagocytic cells (macrophages) loaded with fragments of erythrocytes. The *spleen* is usually pigmented and in many cases it is more or less enlarged. Occasionally, it weighs 1500 grams or more. Microscopically, it may show little deviation from the normal, but not rarely the pulp is found to be hyperemic and to contain increased numbers of large phagocytic cells. The lymph-nodes, especially the hemolymph-nodes, share in the general siderosis and usually show in their dilated sinuses many phagocytes. *Hypertrophy of*

[1] Addison: On the Constitutional and Local Effects of Disease of the Suprarenal Capsules, 1855.

[2] Correspondenzbl. f. Schweiz. Aerzte, 1872, No. 1.

[3] William Hunter: Severest Anemias, Macmillan & Co., Ltd., 1909.

*the heart*, more or less pronounced, was observed at necropsy in 18 of 19 cases at the Massachusetts General Hospital (Cabot and Richardson[1]). Degenerative changes are found in the *spinal cord* in more than three-fourths of all cases. The lesions show a predilection for the posterior columns, although eventually the pyramidal tracts usually become involved also, the type of degeneration known as subacute combined sclerosis resulting (see p. 991).

**Pathogenesis.**—Pernicious anemia is due to the activity of a hemolytic poison, the nature and origin of which are still unknown. The evidences of excessive hemolysis are found in the accumulations of iron-containing pigment in the viscera and in the presence of numerous phagocytes filled with the debris of red cells in the lymph-nodes, spleen, etc. Evidently the bone-marrow is also implicated by the hemolysin, the primary effect upon it being increased activity with reversion to the embryonal type of erythropoiesis and the ultimate effect, complete exhaustion of the erythropoietic function. The part played by the spleen is very obscure, but the good results of splenectomy in certain cases indicate that derangement of its function may be one of the links in the chain of factors causing the disease. Apparently the specific poison either directly or indirectly intensifies the normal hemolytic activity of the organ. Eppinger believes that the increased hemolysis occurs in the sinuses of the pulp, into which the blood is diverted owing to thickening and partial occlusion of the follicular arteries. The changes in the spinal cord are undoubtedly the result of the toxemia rather than of the severe anemia itself and may occur in advance of the other manifestations.

**Symptoms.**—The symptoms develop insidiously and vary in the order of their appearance. In the majority of cases, however, the earliest complaint is of muscular weakness, dyspnea or pallor. Less frequently, the initial manifestations are gastrointestinal disturbances, and occasionally symptoms referable to the nervous system, especially to changes in the spinal cord, are the first to attract attention. In the course of time, irrespective of the mode of onset, impairment of muscular power, pallor and edema of the lower extremities become conspicuous features, although occasionally patients retain a remarkable degree of strength and a good color long after the blood has shown marked deterioration.

The *skin* instead of presenting the white, death-like appearance commonly seen in severe anemias is usually of a peculiar lemon-yellow tint. In some instances there is actual jaundice, and very rarely areas of brownish pigmentation, suggesting Addison's disease, make their appearance. Notwithstanding the increasing pallor and asthenia, the *patient's weight* is, as a rule, well maintained; indeed, from the combination of plumpness with the peculiar yellow pallor the existence of the disease may often be suspected at first sight. During active periods of the disease paroxysms of *fever* (100°–102° F.), lasting from a few days to two or three weeks, occur in at least 80 per cent. of the cases. *Basal metabolism* is usually distinctly above the normal level (Meyer and Dubois,[2] Mosenthal[3]).

The *circulatory disturbances* are those common to other forms of profound anemia, namely, dyspnea, dizziness, tinnitus, palpitation, visible pulsation of the vessels, hemic murmurs over the heart and at the root of the neck, edema, etc. Retinal hemorrhages, purpura, and bleeding from the mucous membranes may occur, but the last is somewhat uncommon. *Gastrointes-*

[1] Jour. Amer. Med. Assoc., April 5, 1919.
[2] Archives Int. Med., 1916, xvii.
[3] Johns Hopkins Hosp. Bull., 1918, xxix.

*tinal derangements* are a cause of complaint in a large proportion of cases. The most frequent are anorexia, nausea or vomiting and diarrhea, or perhaps constipation, or alternating constipation and diarrhea. Whatever their nature, the gastrointestinal symptoms are likely to be paroxysmal and to prove resistant to treatment. The *tongue* is often abnormally sensitive, red, smooth and excoriated, but these changes are neither constant nor characteristic. Examination of the *gastric juice* almost always reveals anacidity and absence of pepsin. Levine and Ladd[1] found persistent anacidity in 99 per cent. of 104 consecutive cases of pernicious anemia at the Johns Hopkins Hospital. Analyses of the duodenal contents, collected by means of an Einhorn tube, show abnormally large values for urobilin and urobilinogen (Schneider, Giffin, Sanford, Szlapka[2]), indicating apparently an excessive degree of blood destruction. The *feces* also contain an abnormal amount of urobilin and urobilinogen. Slight or moderate enlargement of the *spleen* is frequently observed, and occasionally the organ may extend almost to the level of the navel. Slight enlargement of the *liver* is also common. The *urine* is usually pale, but occasionally it is dark owing to an excess of urobilin. In many cases it contains a small amount of albumin and a few casts.

*Nervous symptoms* follow, develop coincidently with, or precede the anemia in the large majority of cases. These may consist merely of abnormal sensations, such as numbness and tingling, etc. but in more than three-fourths of all cases there are important indications of changes in the spinal cord, the symptom-complex pointing to posterior sclerosis, to lateral sclerosis, or much more frequently, to combined sclerosis. Evidences of peripheral neuritis, apart from the paresthesias, may also appear. The most common findings are impairment of vibratory and joint sensibility over the lower part of the body, more or less impairment of superficial sensibility, disturbed coördination, exaggeration or decrease of the patellar and tendo-achillis reflexes and a positive Babinski sign. There is no close relation between the intensity of the nervous phenomena and the degree of anemia and occasionally the former antedate the onset of the anemia by a long period of time. *Mental disorders* are uncommon, but delirium, psychoses of the melancholic type, and delusional states have been described. Definite evidences of *multiple neuritis* were present 4.0 per cent. of 150 cases studied by Woltman[3] at the Mayo Clinic. Multiple hemorrhages occur in the *retina* at one time or another in at least 50 per cent. of the cases.

The *blood* is abnormally fluid and, owing to reduction of the cell mass, the total quantity is diminished. The number of red cells is greatly reduced, the count usually being less than 2,000,000 when the patient first comes under observation. Counts between 500,000 and 200,000 are not very rare. The percentage of hemoglobin is also markedly decreased, although usually it is relatively less reduced than the number of red corpuscles, the color-index, therefore, being high (1.0 to 1.6). This high color-index, which is somewhat characteristic, is due to the presence of many abnormally large cells rich in hemoglobin. The red cells show marked variations in size (anisocytosis) in shape (poikilocytosis) and in staining reactions (polychromasia). Although microcytes are rarely absent, macrocytes predominate, and hence the average diameter of the red corpuscles is increased, which is another important indication. Among the misshapen corpuscles oval and pear-shaped forms are especially prevalent.

Nucleated red cells are to be found in the blood at some time or other in

[1] Johns Hopkins Hosp. Bull., 1921, xxxii, No. 366.
[2] Amer. Jour. Med. Sci., 1918, clv, No. 4.
[3] Amer. Jour. Med. Sci., Mar., 1919.

nearly every case. They may be present in very large numbers, but not rarely their demonstration requires protracted search, and during remissions they may be absent for weeks or months. Especially important from the diagnostic viewpoint is the predominance of megaloblasts over normoblasts, even when the whole number of red cells is small. Accompanying the megaloblasts there is often a high percentage of reticulated cells (skeined cells), as shown by vital staining.[1] The leucocyte count is usually below normal—5000 or less. The reduction affects chiefly polymorphonuclear forms, so that the lymphocytes are relatively increased. Eosinophilia is not uncommon. In Levine and Ladd's[2] series of 150 cases 54 showed 5 per cent. or more of eosinophiles at one time or another. A few myelocytes are frequently found. Near the end there may be a pronounced leucocytosis, due to increase of lymphocytes or more rarely of myelocytes. The number of blood-platelets is usually low.

**Prognosis and Course.**—Pernicious anemia is probably always fatal. It lasts from a few months to ten or even fifteen years. The course is not, as a rule, steadily downward, but interrupted by remissions, which occur spontaneously or are seemingly produced by treatment, and which may last for months or for years. In Stockton's[3] case the disease recurred 20 years after its inception and after 12 years of apparently good health. The remissions may occur even when the red-cell count is as low as 300,000 and the patient is apparently *in extremis*. The improvement which is sometimes remarkably rapid, often begins at the close of a paroxysmal attack of vomiting or diarrhea. In many cases it becomes so pronounced that the patient feels entirely well and is able to resume his usual occupation. As regards the blood, early indications of improvement are an increase not only in the number of erythrocytes and percentage of hemoglobin, but also in the number of leucocytes, especially of the polymorphonuclear forms, a lowering of the color-index, and a replacement of the megaloblasts by normoblasts. Although there may be several remissions in a single case, a relapse sooner or later occurs that precedes a fatal termination.

**Diagnosis.**—Except in the initial stage and during remissions, pernicious anemia is, as a rule, easily recognized. Although neither the clinical findings nor the blood changes are in themselves absolutely distinctive, nevertheless the summation of these data, together with the patient's history and a careful observation of the course of the disease, will almost always lead to the correct diagnosis. Important diagnostic features are the insidious onset without recognizable cause, the peculiar color of the skin, the relatively good preservation of fat, the paroxysmal occurrence of gastrointestinal disturbances, the presence of symptoms referable to lesions in the spinal cord, the tendency to spontaneous remissions, and in the blood the extraordinary reduction in the number of red cells without a corresponding reduction in the amount of hemoglobin, the decrease in the number of leucocytes, especially in the number of polymorphonuclear forms, marked poikilocytosis and anisocytosis with the occurrence of many abnormally large red cells, the presence of nucleated red cells with a predominance of megaloblasts, pronounced polychromatophilia, and a reduction in the number of blood-platelets.

Severe *secondary anemia* may be excluded by the detection of the causative factor (small but frequently repeated hemorrhages, chronic infection,

[1] This consists in staining of blood in the liquid state before it has been acted upon by the air. The reticulum is well stained with brilliant cresyl blue. Normally, about 0.8 per cent. of the red cells are reticulated. In pernicious anemia the percentage varies from 0 to 20, high percentages apparently indicating increased hemopoietic activity on the part of the bone marrow.

[2] *Loc. cit.*

[3] Amer. Jour. Med. Sci., Oct., 1919.

pregnancy, helminthiasis, chronic nephritis, etc.), and also, as a rule, by the blood picture, which, in comparison with that of pernicious anemia, usually shows a less pronounced decrease in the number of red cells, a relatively low, instead of a relatively high, percentage of hemoglobin, few or no oversized red cells, no nucleated red cells or only a few normoblasts, and no leucopenia, but rather an increase in the number of leucocytes, especially of the polymorphonuclear forms. In the *anemia of dibothriocephalus infection*, however, both the clinical and hematologic pictures may be indistinguishable from those of pernicious anemia, so that the diagnosis may have to depend on the discovery of portions of the worm or its ova in the feces. Even the eosinophilia, which is a diagnostic feature in most cases of helminthiasis, often disappears when the anemia becomes severe and moreover eosinophilia is not rare in pernicious anemia. Exceptionally *syphilis* also produces every feature of pernicious anemia, including the blood changes, and therefore a person who seems to have pernicious anemia and who presents definite evidence of syphilis should be given the benefit of antiluetic treatment, although it must be recognized, of course, that syphilis, owing to its great prevalence, must in some cases of severe anemia be merely an associated condition and not the etiologic factor.

*Latent gastric cancer* may closely simulate pernicious anemia, but usually in the former the symptoms are steadily progressive, if gastric disturbances are present, they are persistent, the oligocythemia is not so extreme, the count rarely being below 1,500,000, and the anemia is of the secondary type with a low color-index and an absence of embryonal features, such as megalocytes, megaloblasts, etc. *Purpura hemorrhagica* may have many symptoms in common with pernicious anemia, but the blood, except in the marked decrease of platelets, shows the changes of ordinary, posthemorrhagic anemia, *i.e.*, absence of low color-index, leucocytosis, absence of embryonal features, etc. In *acquired hemolytic icterus*, which at times may resemble pernicious anemia, acholuric jaundice is a constant feature, the gastric chemism is not altered, splenic tumor is a striking feature, symptoms referable to changes in the spinal cord are rarely observed, the fragility of the red blood-cells is increased, the color-index is usually normal, and neutrophilic leucocytosis is often present. The distinctive features of primary *aplastic anemia* are considered on p. 823.

**Treatment.**—Rest is beneficial and during exacerbations it is imperative. An abundance of fresh air and sunshine is important. The diet should be liberal and should consist of nutritious and easily assimilable food, the amount and particular kind being adjusted to the digestive power of the patient. With the view of increasing the bulk of the blood it is sometimes advisable to reinforce the diet with an abundance of milk. Gentle massage is useful, especially when prolonged rest is required. The bowels should be evacuated daily, using for the purpose, if necessary, suitable cathartics or preferably colonic irrigation with salt solution. Focal infection should be sought for in the teeth, gums, nose, paranasal sinuses, urogenital tract, etc., and if found an attempt should be made to remove it, since even if it is not the sole cause of the disease, it may at least be an accessory factor.

As regards special remedies, the reputation of arsenic seems to be well founded. This drug may be administered in the form of Fowler's solution, beginning with 3 minims (0.2 mil) three times a day after meals and increasing 1 minim (0.06 mil) daily until 15 minims (1.0 mil) per dose are taken, provided no symptoms of saturation appear. After continuing for a week with full doses, the drug should be discontinued for several days and then resumed, beginning with one-half the maximum dose and increasing the

amount by increments as before. If the arsenic cannot be taken by the mouth, it may be given in the form of sodium cacodylate by intramuscular injection, using ½ grain (0.03 gm.) once daily for a week and then intermitting the treatment for a week. Arsphenamin has been used with gratifying results in some cases (Bramwell,[1] Boggs,[2] Lampe[3] and others), but its effects are not always good and it is inadvisable to employ it if the hemoglobin is below 25 per cent., as the drug itself causes temporary hemolysis. Iron is either useless or actually deleterious. On account of the gastric anacidity the use of diluted hydrochloric acid in large doses has had many advocates.

If the anemia still progresses and the blood regenerative power seems to be incapable of stimulation by the usual methods, transfusion of fresh unmodified blood that is compatible with that of the patient often proves more effective than any other measure. From 250 to 700 mils may be injected at intervals of a week to a month. If untested blood is employed the first 100 mils should be introduced into the vein very slowly, and the transfusion immediately suspended if untoward symptoms (sensation of tingling in the limbs and of oppression about the precordium, cyanosis and embarrassed respiration) develop. Generally speaking, the earlier transfusion is performed, the better are the results. The measure, however, is never curative and with frequent repetition gradually loses its efficiency.

Finally, in selected cases splenectomy seems to be advisable although it has never proved more than a temporizing procedure. The best results have been observed in comparatively young patients in whom the spleen is moderately enlarged and the blood condition is fairly good, notwithstanding a considerable degree of hemolysis, as shown by high values for blood-derived pigments in the duodenal contents or the stools. The operation is contraindicated by spinal cord symptoms and a count of red cells below 1,500,000, especially if this is associated with signs of bone-marrow exhaustion (absence of erythroblasts, absence of reticulated cells, low percentage of polymorphonuclear leucocytes, etc.). When the anemia is severe several transfusions should be performed as a preliminary measure. Transfusion may also prove useful in case of relapse after operation. The most favorable report on splenectomy is that from the Mayo Clinic,[4] which is based upon 50 cases. The operative mortality was 6 per cent. Of the patients who recovered from operation, 21.3 lived 3 years or longer and 10.6 per cent. survived 4½ years or longer and at the time of the report were still living. The conclusion is that splenectomy prolonged life in at least 20 per cent. of the cases.

## ACUTE APLASTIC ANEMIA

Acute aplastic anemia is a fatal form of anemia, the result, in many instances, of an unknown cause, running a rapid and progressively downward course, and dependent upon degeneration of the bone-marrow and failure of blood formation.

Whether it is a disease of itself, due to primary bone-marrow destruction, or a form of pernicious anemia in which from the first there is absence of the usual compensatory regenerative processes in the bone-marrow is uncertain, but the weight of opinion is in favor of the first of these views. The disease is

[1] Brit. Med. Jour., 1913, i, 1413.
[2] Johns Hopkins Hosp. Bull., 1913, xxiv, 323.
[3] Med. Klin., 1916, xii, 1228.
[4] Collect. Papers of the Mayo Clinic, 1920, 538.

comparatively rare. In 1914 Musser[1] collected reports of 59 cases and added another one.

At necropsy the bone-marrow is yellow, fatty, and devoid of hyperplastic changes. The disease occurs usually between the ages of 15 and 35 years and is somewhat more frequent in males than in females. In some cases it has been due to poisoning by benzol, trinitrotoluene or similar substances, in others it has followed exposure to x-ray or radium emanations for a long time without adequate protection, and in a few instances it seems to have been a result of focal sepsis. In the majority of cases, however, it could not be associated with any definite etiologic factor.

**Symptoms.**—The general symptoms are those common to all rapidly progressing anemias. There is a marked tendency to hemorrhages into the skin and from the mucous membranes and paroxysms of fever are common. Evidences of excessive hemolysis—yellow skin, splenic enlargement, large values for urobilin and urobilinogen in the duodenal contents and feces, urobilinuria, etc.—are wanting. Examination of the blood shows extreme oligocythemia, but, as contrasted with pernicious anemia, no evidences of regeneration of cells. The color-index is low. Nucleated red cells are virtually absent. Macrocytes, poikilocytes and reticulated red cells are absent or few in number. The number of blood-platelets is very low and this probably accounts for the pronounced hemorrhagic tendency. The leucocyte count is usually less than 2000, the polymorphonuclear cells and other granular forms (marrow cells) being absolutely decreased, while the lymphocytes are relatively or actually increased, the percentage not rarely reaching 80 or 90. In some instances the first indication has been an increase of the lymphocytes with a corresponding reduction of the polymorphonuclear cells. The disease is invariably fatal and lasts from 2 or 3 weeks to 1½ years, the average duration being about 6 months.

The diagnosis is not difficult. *Pernicious anemia with exhaustion of the bone marrow* may usually be distinguished by the history of remissions, the color of the skin, high color-index of the red cells, and the presence of a number of large and abnormally shaped red cells. In *purpura hemorrhagica with marked anemia* there is usually leucocytosis with an increased percentage of polymorphonuclear forms, poikilocytosis is often marked, a few normoblasts may be found and the reticulated cells are increased.

**Treatment** of aplastic anemia is unavailing.

## CHLOROSIS

(Green Sickness)

**Definition.**—Chlorosis is a disease occurring in young girls about the time of puberty, and characterized by marked oligochromemia, menstrual disorders and various subjective disturbances.

**Etiology.**—The essential cause of chlorosis is unknown. Of the many hypotheses regarding it, the most satisfactory is that which ascribes the disease to some disturbance of the glands of internal secretion, especially the ovaries (von Noorden, Morawitz, von Jagic). Whatever the nature of the disturbance, it entails an interference with blood production, particularly the formation of hemoglobin, for there is no evidence to show that hemolysis is excessive.

The disease occurs exclusively in females and develops about the time of puberty, that is between the fifteenth and twenty-fourth years, although it may be observed as a relapse or recurrence as late as the thirtieth or even the

[1] Musser, J. H., Jr.: Arch. Int. Med., 1914, xiv, 275.

thirty-fifth year. Chlorosis develops under the most favorable surroundings, but poor hygienic conditions have some predisposing influence. In this country it is most common among servant girls, who have recently come from foreign countries, especially Ireland, who have experienced a sudden change of environment and suffered from home-sickness or other depressing emotions. From some unknown cause the disease appears to be diminishing in frequency.

**Symptoms.**—The symptoms are for the most part those common to all anemias, the patient complaining of muscular weakness, lassitude, headache, breathlessness on exertion, palpitation, attacks of faintness, digestive disturbances and disorders of menstruation. Distress after eating is very common, and may culminate in vomiting; the appetite is poor or morbid in its preference for certain articles of food or even for substances not suitable for food; and constipation is the rule. Examination of the gastric contents often reveals hyperacidity. Pain in various parts of the body, insomnia, and emotional anomalies, as well as signs of vasomotor instability, such as coldness of the extremities, sweating of the hands, etc., are frequent attendants upon the disease. Menstrual disorders, with a tendency toward amenorrhea rather than menorrhagia, are virtually always present. The secondary sexual characteristics are, as a rule, well developed. By degrees the complexion becomes of a pale sickly hue, or sometimes of a faintly yellowish or greenish color, which has suggested the name of the malady. Exceptionally, however, the cheeks are ruddy, even though the anemia is marked (*chlorosis rubra*).

In contrast with the patient's subjective complaints and usual co loring, there is seldom any emaciation; indeed, some chlorotics become stouterduring the course of the disease. The apex-beat of the heart is usually distinct and more diffuse than in health. In marked cases a soft blowing systolic murmur is heard at the apex or base, or both, and a continuous hum (bruit de diable) is audible over the veins of the neck. An increased area of cardiac dulness (dilatation) is often shown on percussion. Edema of the feet and ankles or puffiness beneath the eyes is common. Slight fever is often noted. Save for the presence of a trace of albumin, the urine shows no changes of importance.

*The Blood.*—The total amount of plasma is decidedly increased (polyplasmia), and the drop of blood as it flows from the puncture is pale, but the characteristic feature is the marked reduction in the quantity of hemoglobin. The number of red corpuscles is, as a rule, approximately normal or only moderately decreased (4,500,000 to 3,500,000), whereas the hemoglobin usually varies from 60 to 40 per cent. The color-index is obviously low, the average being about 0.5. Many of the cells are of small size and some are deformed. In severe cases a few nucleated red cells, chiefly normoblasts, may be present. The leucocytes are usually normal in number, but there may be a slight relative lymphocytosis. Severe cases are occasionally observed in which the red-cell count falls to 2,000,000 or even 1,500,000 and the hemoglobin to 30, 20, or even 10 per cent. On the other hand there are mild cases in which the subjective symptoms are distinctive, but the blood changes are extremely slight (*larval form*).

**Complications.**—Not a few chlorotics present definite signs of gastroptosis. An abortive Basedow's syndrome is occasionally observed. Gastric ulcer has been reported somewhat frequently. In many of the cases, however, the diagnosis seems scarcely to have been justified by the evidence. Chlorosis is believed by some to favor the development of tuberculosis, but a critical decision in the matter is difficult, owing to the fact that incipient tuberculosis with secondary anemia may easily be mistaken for chlorosis.

Thrombosis of the veins is not a very rare complication (1 to 2 per cent. of the cases). By far the commonest site is the lower extremities, but the veins of the arms or the cerebral sinuses are sometimes involved. In 52 cases affecting the lower extremities, reported by Leichtenstern,[1] pulmonary embolism occurred in 10. The cause of chlorotic thrombosis is not definitely known. Apparently the clotting is not due to any increase in the fibrin content of the blood. Neuroretinitis has been reported as a complication by a number of writers. In several cases the changes in the fundi were so marked that they were mistaken for the neuritis of brain tumor.

**Diagnosis.**—This is based on the age and sex of the patient, the association of marked pallor with an apparently good condition of general nutrition, the menstrual anomalies, and the combination of marked oligochromemia with slight or moderate oligocythemia. Care must be taken not to mistake for chlorosis secondary anemia due to *beginning tuberculosis*, to *chronic nephritis*, or to *peptic ulcer* with recurring small hemorrhages into the bowel. *Neurasthenia* and *hyperthyroidism* sometimes bear a more or less superficial resemblance to chlorosis, but in the former the blood picture is not necessarily altered and in the latter, while there may be a moderate grade of anemia, the diagnosis is likely to be suggested by the more or less constant tachycardia, tremors, physical and mental unrest, loss of weight, tendency to diarrhea, and perhaps, definite enlargement of the thyroid or exophthalmos. It must not be forgotten, however, that chlorosis is occasionally complicated by a mild degree of hyperthyroidism.

**Prognosis.**—The outlook is very favorable. Under appropriate treatment recovery occurs, as a rule, in from 3 to 6 months, but relapses are not uncommon, and occasionally they are repeated over a period of years. A fatal termination is extremely rare; it may occur, however, as a result of thrombosis of the cerebral sinuses or of pulmonary embolism secondary to thrombosis of a peripheral vein.

**Treatment.**—An abundance of sunlight and fresh air, a diet of simple but nourishing food, and, in all but the mildest cases, rest in bed for two or three weeks will do much to hasten recovery. Daily evacuation of the bowels should be procured by regulation of the diet and if necessary by the use of laxatives, of which the best, perhaps, are cascara sagrada, rhubarb, aloes and phenolphthalein.

The specific remedy for the disease is iron, but how this drug exerts its beneficial influence is not known. According to Morawitz it probably acts not so much upon the bone-marrow as upon the basic cause of chlorosis, which seems to be a disturbance of the secretions of ductless glands. One of the most satisfactory preparations of iron is Blaud's pill, one 5-grain (0.3 gm.) pill being given after each meal during the first week, two pills after each meal during the second week, and three pills after each meal thereafter, the treatment being continued for several weeks after the hemoglobin has reached the normal amount. Other reliable preparations of iron are reduced iron, the citrate of iron and the pyrophosphate of iron. If for any reason iron cannot be taken by the mouth, the citrate of iron may be given by intramuscular injection (see page 817). Arsenic in the form of Fowler's solution, 5 min. (0.3 mil), three times a day, or arsenic trioxid, $\frac{1}{40}$ grain, (0.0016 gm.), three times a day, is sometimes a useful adjuvant to iron. If there is anorexia a bitter stomachic, such as nux vomica or gentian, should be given before meals.

[1] Münch. med. Woch., Nov. 28, 1899.

## ERYTHREMIA

(Polycythemia Vera; Vaquez's Disease)

**Definition.**—Erythremia is a comparatively rare chronic disease characterized by persistent and absolute polycythemia, enlargement of the spleen, various nervous symptoms, and a tendency to hemorrhages and to peripheral venous thrombosis.

The disease was first recognized by Vaquez[1] in 1892 and vividly described by Osler[2] in 1903.

**Etiology.**—The cause of erythremia is unknown. The condition is usually first recognized in middle life and males are affected much more frequently than females. A familial tendency has occasionally been noted. Osler believed that the disease is due to a primary hyperplasia of the erythroblastic bone-marrow. Koranyi and Bence[3] have suggested that the causative factor is a lack of oxygen-carrying capacity of the red-blood cells, and that this defect necessitates an excessive production of erythrocytes. Metchnikoff[4] ascribed the condition to a hemolytic toxin, that was too weak to destroy the red corpuscles, but sufficiently active to stimulate the blood-forming organs. Tuberculosis of the spleen has been found in a few instances, and it is obvious that the spleen is always primarily or secondarily involved in the process, but the part that this organ plays is obscure. According to Widal and Eppinger the polycythemia is due to a loss of splenic function.

**Morbid Anatomy.**—The most constant findings are marked congestion of the various organs, enlargement of the spleen in consequence of engorgement of its pulp with red corpuscles, and transformation of the bone-marrow from the yellow to the red variety, with a loss of fat and a hyperplasia of the erythroblastic and, to a less extent, of the leukoblastic tissue.

**Symptoms.**—The cyanosis is usually the most conspicuous feature, the color of the skin, however, is reddish-purple or purplish-red rather than blue. The superficial vessels everywhere are distended, the conjunctivæ are injected, and the veins of the fundus of the eye are enlarged and tortuous. Occasionally, the complexion is normal or somewhat pale and in this event the disease may readily be overlooked unless the blood is examined. The number of red blood-cells is usually between 6,000,000 and 9,000,000, but counts as high as 12,000,000, and even 15,000,000 have been reported. The percentage of hemoglobin is relatively low, the color-index being less than I. The number of leucocytes is about normal or somewhat increased. Occasionally, myelocytes are found in the peripheral blood. The total blood volume exceeds the normal, the viscidity of the blood is much increased, and the bleeding time and the coagulation time are within normal limits. The spleen is, as a rule, only moderately enlarged, but in some instances it reaches to or below the umbilical line. Clubbing of the fingers is occasionally noted.

Nervous symptoms, the result of circulatory disturbances, are rarely absent. The most common are vertigo, headache, buzzing in the ears, paresthesias, neuralgias, blurring of vision, and ready fatigue. Hemiplegia sometimes ensues. Chorea has also been reported (Bordachzi, Pollock[5]).

Hemorrages are common and may occur from the nose, the gums, the kidneys, the bowel, or the lungs, or into the brain. Bleeding was mentioned

[1] Bull. méd., 1892, vi, 849.
[2] Amer. Jour. Med. Sci., Aug., 1903.
[3] Deutsch. med. Woch., 1906, xxxii, 1451.
[4] Quoted by Seufert, Amer. Jour. Med. Sci, Dec., 1910.
[5] Jour. Amer. Med. Assoc., Mar. 11, 1922.

in 10 of 15 cases analyzed by March[1] and in 23 per cent. of 179 cases collected by Lucas.[2]

Cases are not rarely observed (polycythemia hypertonica) in which the arterial tension is high, the heart is large and dyspnea is present, but the spleen is of normal size.

**Diagnosis.**—This is based upon the presence of persistent and absolute polycythemia, chronic cyanosis, and enlargement of the spleen without discoverable cause. Other conditions producing *chronic cyanosis*, such as congenital malformations of the heart, organic disease of the heart, chronic pulmonary affections, especially emphysema, tumor or aneurysm causing stasis of the venous circulation, poisoning by acetanilid, antipyrin, etc., and the rare forms of methemoglobinemia and sulph-hemoglobinemia dependent upon autointoxication of intestinal origin, as well as other conditions producing *polycythemia*, such as chronic disease of the heart or lungs with venous stasis, dehydration of the blood (severe diarrhea, excessive sweating, stenosis of pylorus, etc.), poisoning by carbon monoxid, low atmospheric pressure, etc. must be excluded.

**Prognosis.**—The outlook so far as life is concerned is good, but recovery is unknown. The majority of patients live many years. An acute case of three months' duration, however, has been reported by Türck.[3] Death frequently results from cerebral apoplexy or peripheral venous thrombosis.

**Treatment.**—Venesection often affords relief, but its good effects are only temporary. X-ray or radium treatment of the bones, as suggested by Stengel in 1907, has been of benefit in some instances. In two of Türck's cases Fowler's solution (30 drops daily) was apparently beneficial. Benzol has been recommended, but its effects have not been satisfactory. Splenectomy has not produced favorable results, indeed it is likely that the splenomegaly is a compensatory condition. A restricted diet, hydrotherapy, repeated bleeding and courses of bromids relieve the nervous symptoms.

[1] Med. Clin. of N. America, Nov., 1919.
[2] Arch. Int. Med., Dec., 1912.
[3] Mitt. a. Wien. Geselsch. f. inn. Med., 1902, Nos. 6 and 7.

# THE HEMORRHAGIC DISEASES

## HEMOPHILIA

**Definition.**—Hemophilia is a rare anomaly of constitution, almost always hereditary, characterized by a marked increase in the coagulation time of the blood and a tendency to protracted bleeding after trauma of any kind, even the most trivial. Although the disease has been recognized since the earliest days of medicine, it attracted little attention until the appearance of an important article by Otto,[1] of Philadelphia, in 1803.

**Etiology.**—Hemophilia has been described as the most hereditary of all hereditary diseases (Grandidier[2]). Not rarely it can be traced back through many generations, as is well shown in Legg's[3] record of the Clitherow family, in which it was known to have existed for 200 years. Occasionally, however, it arises spontaneously in a healthy stock, the "bleeder," who in this case is always a male, transmitting the disease to succeeding generations. Although not wholly immune, females are seldom affected, but they possess a much greater capability of transmitting the disease than males. Indeed, women of bleeder families, who are not themselves bleeders, transmit the disease to a majority of their male descendants. However, the view formerly held that hemophilia is transmitted exclusively by females is now known to be incorrect.

The facts regarding heredity may be formulated as follows: Males of bleeder families are very prone to inherit the disease, but virtually never transmit it to their descendants unless they themselves are bleeders. Even males who are themselves affected are much less likely to transmit the tendency than healthy females of hemophiliac parentage. Although daughters of a bleeder, even if healthy, commonly transmit the disease to their male offspring, they sometimes fail to do so. The second generation is usually skipped, and occasionally the descent is interrupted for two generations.

The essential feature of hemophilia is a prolongation of the coagulation time of the blood, which is especially marked in the intervals between hemorrhages. This delay is due, not to any alteration in the number of blood corpuscles or platelets, or in the amount of fibrin and salts, but to some chemical deficiency, the exact nature of which is not definitely known. Sahli advanced the hypothesis that the tardy coagulation is due to an hereditary deficiency in the fibrin-forming substance, thrombokinase, in the vessels walls, so that when the latter are injured there is no local production of fibrin. Howell found evidence of a diminution in the prothrombin in the blood, which necessarily means a relative increase in the antithrombin. The latter holds the prothrombin in combination and prevents its conversion into thrombin, which reacts with fibrinogen to form fibrin. According to Fonio, and Minot and Lee, the blood platelets are deficient qualitatively, although normal quantitatively. In shed blood the platelets and tissue cells

[1] New York Med. Repository, 1803.
[2] Die Hämophilie, Leipzig, 1877.
[3] St. Barth. Hosp. Rep., 1881.

furnish a thromboplastic substance, which opposes the action of antithrombin and thus permits the calcium salts to react with the prothrombin to form thrombin. The bleeding time (see p. 834) in hemophilia is about normal and the blood clot is firm and retracts in normal manner.

**Symptoms.**—In the large majority of cases the disease is made manifest in the first two or three years of life, but occasionally it escapes recognition until puberty or manhood. The first symptom to attract attention is usually protracted bleeding, occurring spontaneously or initiated by some slight injury, such as extraction of a tooth, a cut, puncture, or bruise. The bleeding may occur from any part of the body, but the most common sources of it are the nose, gums and mouth, skin, joints, stomach and intestine. It may continue for hours or days, or may be uncontrollable and terminate in death. Slight contusions often give rise to subcutaneous hemorrhages and the formation of hematomas.

Hemorrhages into the joints, especially the knees or elbows, occur in a large proportion of cases. The blood may be entirely absorbed, but as a rule it persists and leads to an arthritis, which may simulate very closely either acute articular rheumatism or a tuberculous process. In a number of instances operation based upon an incorrect diagnosis has resulted fatally from slow oozing. Ultimately changes may occur in the affected joints resembling those of arthritis deformans, or the condition may terminate in complete ankylosis. At no time is there any tendency to abscess or sinus formation.

Various degrees in the retardation of the coagulation of the blood, and therefore in the severity of the clinical symptoms, are observed. In some cases the patient is never free for any length of time from some manifestation of the disease; on the other hand, there are hemophiliacs in whom hemorrhage is no more readily induced than in normal persons and the only evidence of the anomaly is the tendency of the bleeding to persist. Occasionally the hemorrhagic tendency appears to be limited to certain parts of the body (local hemophilia), such as the mucous surfaces or the kidney, other parts when injured responding as in normal individuals.

**Diagnosis.**—The diagnosis is not often difficult. A hemorrhagic tendency that is due to hemophilia has usually the following characteristics: It is hereditary, it appears at an early date, it is persistent, it is prone to cause hemarthrosis and arthritis, and it is associated with retarded blood coagulation,[1] which is especially marked in the intervals between bleedings. *Chronic purpura hemorrhagica* is rarely hereditary and is characterized by a normal blood coagulation time and by a marked decrease in the number of blood-platelets. Moreover, according to Hess,[2] the application of a tourniquet to the upper arm for a few minutes is productive of minute petechiæ in purpura, but not in hemophilia (capillary resistance test) and subcutaneous puncture of the skin usually causes an area of hemorrhagic extravasation in purpura, but not in hemophilia. In purpura joint symptoms are comparatively rare, superficial ecchymoses are much more common than in hemophilia, and the blood-clot is soft and does not retract. In *familial*

[1] The following method for determining the coagulation time is simple and reliable: Aspirate blood directly from a vein into a syringe coated on the inside with a thin film of a petrolatum-ether mixture, and then expel 2 c.c. into a wide, absolutely clean test-tube. The time elapsing between the moment the blood is drawn and the moment at which an invertible clot is formed is regarded as the coagulation time. The coagulation time of normal blood averages about 20 minutes. Even in hemophilia blood from small needle pricks or from wounds that are not perfectly fresh or blood that has become mixed with tissue juices may clot in the normal time.

[2] Archives of Int. Med., Feb., 1916.

*telangiectasis* (see p. 718) the bleeding is regularly in one location, usually the nose, and is dependent upon an obvious lesion; males are affected as well as females, and the coagulation time of the blood is not prolonged.

**Prognosis.**—The outlook is not favorable. More than half of the 152 cases collected by Grandidier ended fatally before the eighth year. As age advances, however, the bleeding tendency diminishes, and it may cease altogether after maturity. Patients rarely die in the first bleeding and in the lives of many bleeders there are periods of months or years in which the hemorrhagic tendency is lessened or even absent.

**Treatment.**—Members of bleeder families, particularly female members, should be advised not to marry. Hemophilic children should be placed under good hygienic conditions and should be protected, so far as possible, from traumas of all kinds. No operations on them, not even trivial ones, should be undertaken, except for conditions that in themselves may prove fatal. Vaccination by scarification, however, may be performed without misgivings. Residence in a warm climate, especially during the winter, is advisable.

When bleeding occurs rest, compression, and applications of epinephrin, gelatin, tannin, or ice may be tried, although they will usually be found ineffectual. Calcium salts are frequently employed internally, but are rarely of benefit. The best results are obtained from the use of serums or applications of fresh tissues or extracts of tissues, such as brain, thyroid gland, spleen, etc. Serum may be administered intravenously or subcutaneously or applied locally to the bleeding point. Human serum, if it can be obtained, is preferable, but horse serum, even in the form of diphtheritic antitoxin, or rabbit serum may be used. The usual dose for intravenous injection is from 20 to 30 mils, repeated daily if necessary. Thromboplastin in the form of an extract of brain (kephalin) or an extract of blood-platelets (coagulen), applied locally to bleeding wounds, has been found effective. In very obstinate cases the indications are best met by blood transfusion (100 to 500 mils). Unmodified blood is preferable, but before it is transfused, tests for agglutination and hemolysis, and for syphilis should, of course, be made.

Recent hemarthrosis should be treated by rest and moderate compression, or, if the effusion is large, by aspiration with a fine needle, followed by the application of a pressure bandage. After several days gentle massage is indicated.

## PURPURA

Purpura is a condition characterized by hemorrhages into the skin and mucous membranes. When there is also free bleeding from one or more of the mucous surfaces the condition is known as purpura hemorrhagica. In the large majority of cases the hemorrhagic tendency is clearly symptomatic of some underlying morbid state. In a small group of cases, however, the primary cause is not recognizable and the hemorrhages are the dominant clinical feature. Hence, as in the anemias, we speak of secondary purpura and primary purpura. This classification is serviceable for clinical purposes, but must not be regarded as final, for it seems certain that as we become better acquainted with the causation of purpura the number of cases assigned to the primary group will progressively diminish.

The purpuric lesions, which usually appear in successive crops, may be in

the form of petechiæ (round or oval spots from 1 to 3 or 4 mm. in diameter), ecchymoses (larger areas, often irregular in outline), or vibices (hemorrhagic streaks of varying length). When fresh the extravasations are bright red in color, but after a few days the larger ones usually undergo the color changes of a bruise, becoming in turn bluish, bluish- or greenish-yellow, yellowish-brown, and finally disappearing. Any part of the body may be affected, but the legs are most frequently involved, probably because in many instances venous stasis is a contributing factor.

**Secondary or symptomatic purpura** may occur in a great variety of conditions, which provisionally may be classified as follows: (1) *Infectious diseases.* A purpuric eruption is commonly present in typhus fever, and may occur also in cerebrospinal fever, smallpox, measles, scarlatina, and general streptococcus and staphylococcus infections. In subacute streptococcus endocarditis petechiæ are found in more than 75 per cent. of the cases. In some cases of meningococcus sepsis subcutaneous hemorrhages appear before the occurrence of meningitic symptoms or without any involvement of the meninges and are regarded as evidence of a primary fulminating purpura. (2) *Cachectic states*, such as develop in scurvy, pernicious anemia, leukemia, carcinoma, chronic nephritis, etc. (3) *Certain intoxications*, notably poisoning by iodids, salicylates, copaiba, arsenic, antipyrin and benzol. Selling[1] has reported 7 cases of grave anemia of the aplastic type, with purpura, due to benzol poisoning. Apart from drug poisoning, jaundice, anaphylaxis, and snake-bite may also cause purpura. (4) *Certain diseases of the liver.* Extensive destruction of the parenchymatous tissue of the liver, such as occurs in acute yellow atrophy, phosphorus-poisoning, delayed chloroform-poisoning, and advanced cases of cirrhosis are frequently characterized by purpura. 5) *Old age.* Senile purpura is usually observed on the legs, especially about the ankles. It is of local origin and apparently the result of degenerative changes in the peripheral veins. (6) *Obstructed circulation.* Purpura from this cause may occur about tight bandages or after epileptic seizures or paroxysms of whooping cough. (7) *Nervous disorders.* The purpuras that have rarely been observed in neuralgia (in the areas of pain), as an accompaniment of the lightning-pains of tabes dorsalis, and perhaps in hysteria belong to this group.

**Primary Purpura.**—For clinical purposes the so-called primary purpuras are usually classified as follows: (1) Simple purpura; (2) Arthritic purpura (Schönlein's disease); (3) Visceral purpura (Henoch's purpura); (4) Purpura hemorrhagica (morbus maculosus of Werlhof). Whether all of these clinical forms are separate disease entities is doubtful. It is probable that the second and third forms, at least, are identical, differing from each other only in degree. The frequency with which intermediate forms are observed lends support to this view. Purpura hemorrhagica, being associated with definite blood changes, may for the present be regarded as a disease by itself, although it must be admitted that cases are at times observed which suggest a possible relationship of this form of purpura to that of Henoch. It is quite possible that simple purpura is but a mild form of one of the other main varieties.

**Etiology and Pathogenesis of Purpura.**—While the etiology of secondary purpura is obvious in many cases, that of the primary form is entirely unknown. An infectious origin has been surmised, but thus far bacteriologic studies have yielded no definite results. Autointoxication the result of faulty metabolism has also been suggested as a possible cause. The fact that many of the manifestations of visceral purpura correspond very closely to those of anaphylaxis has led to the belief that this form of purpura, at

[1] Johns Hopkins Hosp. Bull., 1910, xxi.

least, may be an expression of supersensitiveness to certain protein substances.

As regard the immediate cause of the hemorrhagic extravasations, different factors are probably operative in different cases. Flexner has shown that snake venom contains a substance, hemorrhagin, which is highly destructive to the endothelial cells of the capillaries, and reasoning from analogy, it seems likely that there may be other poisons capable of producing purpura by setting up degenerative lesions in the blood-vessels. Doubtless senile purpura is due to changes in the peripheral vessels. The petechial hemorrhages occurring so frequently in subacute infective endocarditis are apparently due to the plugging of minute vessels with emboli. In many forms of purpura changes in the blood itself seem to be the essential factor. Thus, there is some evidence to show that the hemorrhagic tendency in certain diseases of the liver, such as acute yellow atrophy, depends upon a deficiency of fibrinogen, an element of the circulating blood that is produced in the liver, and the results of the clinical studies of Denys, Hayem, Duke and others leave little room for doubt that a diminution in the number of the blood platelets is directly responsible for the hemorrhages occuring in purpura hemorrhagica. The platelets are an important factor in the arrest of capillary bleeding, not only on account of their agglutinative power, but also because they are an important source of prothrombin and thromboplastin. There is some evidence that the tendency to bleed occurring in obstructive jaundice is due to an abnormality in the blood calcium. This element does not appear to be deficient in quantity, but unavailable for coagulation because the bile pigments have combined with it.

## PRIMARY PURPURA

**Simple Purpura.**—This, the mildest form of the disease, is most common in adult life. The occurrence of purpuric spots on the limbs, most frequently the legs, is as a rule, the only symptom. Occasionally, however, there is slight articular pain. The condition usually lasts about 2 weeks, but in some instances new lesions appear at intervals for several weeks, and exceptionally the tendency persists for years.

**Arthritic Purpura (Schönlein's Disease.)**—This form is often spoken of rheumatic purpura, but there is no evidence that it is in any way related to true rheumatism. The purpuric eruption is similar to that of simple purpura, but in addition there is an arthritic element, involving, as a rule, several joints and characterized by pain, tenderness, and swelling. In the majority of cases fever, slight or moderate, is also present, and not uncommonly the disease begins with symptoms of sore throat. Occasionally, other skin lesions, such as those of urticaria (purpura urticans) or erythema multiforme, are associated, and in rare instances there is a vesicular or bullous eruption, suggestive of pemphigus (pemphigoid purpura). Endocarditis is very exceptional. Recovery is the rule, but recurrences at yearly intervals are sometimes observed.

**Visceral Purpura (Henoch's Purpura).**—This term is applied to a group of cases having in common various skin lesions of an erythematous or exudative type, such as erythema multiforme, purpura, urticaria and angioneurotic edema, in association with certain visceral manifestations, which are dependent also upon local congestion, hemorrhage or serous transudation. Willan, in 1808, first drew attention to the occurrence of visceral symptoms in a case of purpura; Henoch, in 1874, described similar cases more fully, and Osler,[1] in 1904, reported a large series of cases, emphasizing their common

[1] Amer. Jour. Med. Sci., Jan. and May, 1904.

basis. The condition is observed most frequently in children, although it may occur at any age. Recurring attacks at long or short intervals, over periods ranging from several weeks to many years, are the rule.

The *skin lesions* are protean in type, appear in various combinations, and vary not only in different attacks, but in the course of the same attack. They consist of simple erythema, erythema multiforme, erythema nodosum, erythema urticans, purpura, urticaria, angioneurotic edema, and pemphigoid eruptions. Lesions of the erythema group are the most common. Occasionally the local infiltration of blood and serum is so intense that it results in sloughing. *Arthritis* is often present. The most common of the *visceral manifestations* are gastrointestinal attacks, consisting of colicky pains, vomiting and diarrhea, and hematuria or disturbances of the renal function indicating actual nephritis. In some instances the colicky pains are very severe and are accompanied by the passage of mucous and blood in the stools, so that not rarely operations have been done for supposed intussusception or appendicitis. Indeed, as a result of local infiltration in the bowel wall, intussusception may actually occur, as in cases reported by Tonking, Lett, Barling[1] and others. In some attacks of visceral purpura there are no skin lesions, and when this is the case the diagnosis is especially difficult. Less common manifestations of the disease are bleeding from the nose, mouth or stomach, enlargement of the liver and spleen, attacks of hemiplegia (usually transient) and hemorrhages into the eye, sometimes resulting in ophthalmitis.

There are no changes of importance in the blood. The attack usually terminates favorably within two or three weeks, but death may occur from nephritis or more rarely from hemorrhage into the brain or from intestinal obstruction, the result of a massive hemorrhage into the intestinal wall. In 5 of Osler's[2] cases death occurred from uremia. In patients who recover chronic nephritis is rarely seen, although the albuminuria may persist for months. The *diagnosis* of Henoch's purpura is sometimes difficult, especially when the visceral manifestations are unaccompanied by skin lesions. In suspicious cases the presence of joint-pains or slight hematuria and a history of previous attacks of purpura, urticaria etc., are important.

**Purpura Hemorrhagica (Morbus Maculosus of Werlhof).**—In this form bleeding from the mucous surfaces is a conspicuous feature. Nasal and oral hemorrhages are especially common, and bleeding may occur also from the kidneys, uterus, bladder, stomach or bowel, or, more rarely, into the brain or retinæ. Cutaneous hemorrhages, pectechial or ecchymotic, are usually, but not invariably, present. Even when purpuric lesions of the skin do not appear spontaneously, bruises are likely to be induced by insignificant trauma. Puncture of the skin results in definite subcutaneous hemorrhage, and the application of a tourniquet to the arm is followed by the appearance of petechial hemorrhages. Arthritic symptoms may occur and occasionally there are evidences of nephritis. Fever occurs in more than half of the cases. The coagulation time of the blood is normal or but slightly prolonged (see p. 830); the bleeding time[3] is much prolonged; and retraction of the blood clot with extrusion of serum occurs only after a long time or not at all. The distinctive feature of the blood, however, is the marked decrease in the number of platelets, the count often being below 1000.[4] Leucocytosis is usually present.

[1] Brit. Med. Jour., Mar. 29, 1913.

[2] Amer. Jour. Med. Sci., Dec., 1895.

[3] This is determined by blotting upon absorbent paper all the blood which flows from a small incision at intervals of 30 seconds, and noting the total duration of the bleeding. The bleeding time is independent of the coagulation time and normally varies from 1 to 3 minutes.

[4] The normal count is from 225,000 to 350,000.

Although the loss of blood may be large and the anemia, in consequence, severe, recovery usually occurs within a few weeks, but recurrences, often at long intervals and over periods of many years, are common. Indeed, what appears to be an acute attack is in many cases really a recurrence following a protracted free interval. Apart from this intermittent type there is a rarer chronic form in which the symptoms continue uninterruptedly, but with varying degrees of intensity, for months or even years. On the other hand a malignant form is occasionally observed, in which the bleeding is exceedingly severe and continues almost without cessation until death, which occurs in from a few days to a fortnight (purpura fulminans).

Occasionally purpura hemorrhagica is both hereditary and congenital. It is likely that some of the reported cases of purpura fulminans have been examples of meningococcus sepsis without meningitis (Lereboullet and Cathala, Netter, Herrick).

*Secondary purpura* may usually be distinguished from primary purpura hemorrhagica by the symptoms of the underlying condition and also by the absence of any reduction in the number of blood-platelets. The resemblance to *acute leukemia* is sometimes close, but in this disease the lymph-nodes are usually enlarged, and the blood shows an excess of small or large mononuclear leucocytes and no reduction in the number of platelets. The distinguishing characteristics of *hemophilia* are considered on p. 830; of *scurvy*, on page 347; and *aplastic anemia*, on page 824.

**Treatment.**—Mild forms of the disease require no special treatment. In severe cases rest in bed is of prime importance. Many remedies have been recommended, but only a few are worthy of consideration. In some instances oil of turpentine seems to be of service. Calcium chlorid, 20 grains (1.3 gm.), three times a day, has been extensively used on the advice of Sir Almroth Wright, but there is no evidence that it is of value unless the hemorrhagic tendency is due to a lack of available calcium in the blood, and this appears to be the case only in obstructive jaundice. Subcutaneous injections of fresh blood serum, 30 mils daily, although favorably reported upon by some clinicians, is usually of little avail. The best results are secured by the transfusion of whole blood, which contains all the elements concerned in clotting. In many cases this measure brings about a prompt cessation of the bleeding.

Of local hemostatic remedies, the best, perhaps, are kephalin, an extract of brain tissue, and coagulen, an extract of blood platelets, both of which are rich in thromboplastin. The intravenous use of these agents has also been proposed, but it is by no means devoid of danger. Coagulen, (5 grams in 300 mils of saline solution) however, may be safely given subcutaneously. Stephan[1] reports a case of purpura fulminans which was successfully combated by means of deep roentgenotherapy applied to the spleen.

## HEMORRHAGIC DISEASES OF THE NEWBORN

The hemorrhagic tendency is occasionally observed in the newborn. Bleeding from the gastrointestinal tract is most common (melena neonatorum), but it may occur from the nose, mouth, umbilicus or bladder, or into the skin and mucous membranes. Jaundice is present in many of the cases. Extensive fatty degeneration of the viscera is not rarely found post-mortem, and when this is the case the condition is sometimes spoken of

[1] Münch. med. Woch., 1920, lxvi, No. 11.

As Buhl's disease, although the latter does not appear to be a distinct entity. The etiology of the bleeding is frequently obscure. Roughly the cases may be grouped into those due to: (1) syphilis; (2) septic infection; (3) Winckel's disease; (4) eclampsia in the mother; (5) morbus maculosus neonatorum; (6) hemophilia; (7) trauma during birth. Syphilis and septic infection are responsible for the majority of cases. The disease described by Winckel[1] is an acute epidemic infectious process, occurring chiefly in institutions, characterized by hemoglobinuria, icterus, diarrhea and fever, and attended with a very great mortality. Twenty-three of the 24 cases reported by Winckel ended fatally. Eclampsia in the mother affects the infant in a large proportion of cases. As transmitted to the offspring the intoxication may be manifested by the icterohemorrhagic syndrome, with fatty changes in the liver and multiple thromboses and hemorrhages in the various organs. The term morbus maculosus neonatorum is applied to cases of hemorrhage in the newborn for which no cause can be assigned, and which clinically conform to cases of so-called idiopathic purpura hemorrhagica of adults. In some instances of this group the circulating blood has been found deficient in prothrombin (Whipple, Hurwitz[2]).

Transfusion of whole blood and subcutaneous injection of fresh serum are the only measures which have proved to be of value in the treatment of these diseases. Kephalin or coagulen (see p. 831) may be applied directly to bleeding points, if these are accessible.

[1] Deutsch. med. Woch., Bd. v, S. 303, 1879.
[2] Amer. Jour. Med. Sci., Nov., 1917.

# DISEASES OF THE SPLEEN

## CONGENITAL MALFORMATIONS AND MALPOSITIONS OF THE SPLEEN AND MOVABLE SPLEEN

In rare instances, usually in association with other congenital defects, the spleen is absent or is represented by several, small scattered masses of splenic tissue (splenunculi). Much more frequently splenunculi are present in addition to the normal organ (11 per cent. of all necropsies[1]). Abnormalities of shape, including marked lobulation, are sometimes observed. Rolleston describes a remarkable malformation in which the spleen gave off a long process extending down into the scrotum. In true dextrocardia the spleen is usually on the right side of the abdomen and the liver on the left. In diaphragmatic hernia the spleen is not rarely in the left pleural cavity.

**Movable Spleen.**—Movable spleen, or splenoptosis, is most frequently seen in persons with general visceroptosis, but even in this condition it is rare. Occasionally it occurs without obvious displacement of the other abdominal viscera. Congenital relaxation of the splenic ligaments, deficiency of intra-abdominal support from over-stretching of the abdominal wall, traction by other misplaced organs, and increased weight of the spleen are regarded as important etiologic factors.

Subjective *symptoms* may be entirely absent, or there may be a sense of weight in the back and side. Disturbances of adjacent organs, as a result of pressure or traction, are sometimes observed. Neurasthenic phenomena are not uncommon. The spleen is usually found a little below its normal position, but in exceptional cases it may be as far down as the pelvis. Owing to some preexisting condition or to venous engorgement following the displacement, the organ is, as a rule, enlarged. Twisting of the pedicle may result in intense congestion of the spleen, and, perhaps, perisplenitis, or in thrombosis of the splenic vein. Extensive necrosis of the organ has also been known to occur. Durso[2] collected 26 cases of ectopic spleen from the literature and found that infarction of the entire organ had occurred in 7. Surgical treatment (splenopexy or splenectomy) is indicated in splenoptosis only if the symptoms are severe and do not yield to general hygienic measures and suitable mechanical support.

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## ACUTE SPLENIC TUMOR

This term is applied to the tumefaction of the spleen occurring in many of the acute infectious diseases. The exact nature of the process is somewhat obscure. The changes appear to be brought about partly by the action of bacteria or their toxins and partly by the presence of débris resulting from the disintegration of red corpuscles. The organ is enlarged, sometimes weighing 800 grams or more; its capsule is tense and its substance is soft.

[1] Adami and Nicholls: Prin. of Pathology, Phila., 1909, ii, p. 222.

[2] Studio clinico e sperimentale dello infarto splenico nella rotazione della milza; Policlinico, Rome, 1896, 3 C, 63.

On section it is usually of a pinkish-gray color, except in typhoid fever and allied conditions, in which it is of deep red hue. In some cases the Malpighian bodies are almost hidden by the swollen pulp, but in others they are large and conspicuous.

According to Evans,[1] who has made a special study of the subject, the red and gray types are histologically more or less district. The red type shows a hyperplasia of the endothelial cells of the pulp, with the formation of numerous large phagocytes containing red blood cells and débris, while in the gray variety there is in place of the endothelial proliferation of the pulp an accumulation of pulp cells, especially the oxydase—containing myeloid elements. Areas of necrosis may be found in both types, but are more common in the first. As the primary disease subsides, the spleen usually regains its normal size and appearance, although not rarely some fibrous overgrowth remains as a result of an inflammatory reaction.

**Symptoms.**—Enlargement of the spleen is often the only clinical feature. Local discomfort and tenderness on palpation are sometimes present, and occasionally, probably in consequence of perisplenitis, there is actual pain in the splenic region. In patients with aortic insufficiency an acute splenic tumor has rarely been observed to pulsate (Gerhardt, Prior, Drasche).

## CHRONIC VENOUS CONGESTION OF THE SPLEEN

Chronic venous congestion of the spleen occurs in obstruction to the portal circulation, most frequently in cirrhosis of the liver, but also in certain valvular lesions of the heart, emphysema, etc. The organ is enlarged, of variable consistence, and of a dark-red or purple color. The capsule is usually thickened. Section reveals distention of the veins and more or less pigmentation from disintegration of red blood-cells. After long continuance of the process the organ becomes firm and tough, owing to hyperplasia of the interstitial supporting tissue and secondary condensation and atrophy of the pulp (*cyanotic induration*).

**Symptoms.**—Enlargement of the spleen is the only constant symptom, although a sense of weight or fulness in the region of the spleen is a frequent complaint. The treatment is that of the primary disease.

## EMBOLISM, THROMBOSIS AND INFARCTION OF THE SPLEEN

**Embolism** of the splenic artery has its most common source in acute or chronic valvular disease of the heart and in pyemic processes. It may also arise, however, from cardiac thrombi, atheroma of the aorta, etc., and occasionally it follows thrombosis of the splenic artery. The result is simple infarction (hemorrhagic or anemic) or, in the case of an infective embolus, infarction with ensuing abscess formation. *Clinically*, infarction may manifest itself by pain and tenderness in the left hypochondrium, (perisplenitis), by greater or less enlargement of the spleen, and in some cases by a palpable or audible friction-rub. Occasionally, there is also vomiting of blood. Chills, fever, sweats, etc. may occur if the infarction is transformed into an abscess.

[1] Johns Hopkins Hosp. Bull., 1916, xxvii, 356.

**Thrombosis** of the splenic vein may result from the extension of a thrombus in the portal or mesenteric veins; it may develop in the course of local inflammatory conditions, acute infections or cachectic states; or it may arise from sclerosis or calcification of the walls of the splenic vein itself. Chronic endophlebitis with thrombosis is common in certain forms of splenomegaly and is regarded by a few clinicians as the immediate cause of Banti's symptom-complex. Thrombophlebitis of the splenic vein usually results in congestion and enlargement of the spleen, with a clinical picture indistinguishable from that of splenic anemia. Occasionally, if the process is very acute **infarction** and extensive necrosis of the spleen may occur. Nuzum[1] has collected from the literature 28 cases of infarction of the entire spleen and added 4 cases of his own. Thrombosis of the splenic vein was the most common causative factor.

## ABSCESS OF THE SPLEEN

Abscess of the spleen is comparatively rare. Dege,[2] in 1906 collected 80 cases. Occasionally it occurs as a primary condition, developing without obvious cause or in consequence of trauma. As a rule, however, it results from the direct extension of a suppurative process in an adjacent organ or from the lodgment of an infective embolus in the course of some pyogenic infection, most frequently, perhaps, ulcerative endocarditis. In rare instances it occurs as a complication of one of the specific infections, especially malaria, typhoid fever, or relapsing fever. The **symptoms** are usually overshadowed by those of the primary condition from which the abscess arose. Suggestive features are indications of local peritonitis, with enlargement and tenderness of the spleen, and the usual phenomena of suppuration —remitting fever, sweats, chills leucocytosis, etc. Fluctuation can rarely be elicited. Occasionally, there is edema over the lower intercostal spaces. The abscess may burst into the lung, into one of the hollow abdominal viscera, or into the general peritoneal cavity. In non-embolic cases surgical treatment offers some hope of cure.

## RUPTURE OF THE SPLEEN

Rupture of a normal spleen is almost invariably a result of external violence. Rupture of a diseased spleen may occur in consequence of very slight trauma or even spontaneously. The morbid condition predisposing to this rare event is usually the tumefaction and softening occurring in malaria, typhoid fever, infarct, or abscess. In some instances the accident has resulted from vomiting, coughing, or a sudden turn of the body. In a few cases it has followed puncture by an exploratory needle or rough handling, as in palpation. The chief **symptoms** are sudden, intense pain in the left hypochondrium and abdominal distention, followed very soon by evidences of severe internal hemorrhage and later, if the patient survive, by signs of acute peritonitis. The treatment is essentially surgical.

[1] Jour. Amer. Med. Assoc., Feb. 2, 1918.
[2] Quoted by Doebbelin, Deutsch. med. Woch., 1907, ii, 1346.

## HEMOLYTIC JAUNDICE WITH SPLENOMEGALY

Two forms of this comparatively rare condition are recognized: one, hereditary or congenital and usually familial; the other, apparently acquired. Both forms are characterized by persistent non-obstructive acholuric jaundice usually slight but of varying degree; a marked increase in the output of urabilin; enlargement of the spleen, sometimes reaching huge proportions; and anemia with decreased resistance of the red blood-cells to hypotonic salt solution,[1] and an increase in the percentage reticulated red cells from 5 to 20 per cent., as contrasted with the normal of less than 1 per cent. The concomitants of ordinary obstructive jaundice, such as light-colored stools, choluria, pruritus, etc. are absent, the liver is not at all or only moderately enlarged, and all of the symptoms are subject to marked variations, exacerbations ("crises deglobulization"), sometimes accompanied by fever and always resulting in increased blood destruction, being prone to follow fatigue, indiscretions in diet, excitement, etc. During exacerbations bile may appear in the urine. Gall-stone formation is a frequent complication. It was observed in 7 of 12 cases reviewed by Giffin.[2] Occasionally, one of the important symptoms, such as the increased fragility of the red corpuscles, the splenic tumor, or even the icterus (Chauffard) is absent. The destruction of the erythrocytes probably occurs in the spleen, as splenectomy is followed by marked improvement or actual cure, but the exact rôle that is played by spleen in the disease is not definitely known.[3]

In **chronic hereditary, family, or congenital hemolytic jaundice (Minkowski-Chauffard syndrome)**, which usually dates from birth or is first noticed in adolescence and persists throughout life, the anemia is, as a rule, moderate, and although attacks of indigestion or of abdominal pain, due in some instances to complication with gall-stones, are not uncommon, the general health remains good, the patient being more often icteric than sick (Chauffard). *Congenital obliteration of the bile-ducts* is occasionally familial, but it produces jaundice of an obstructive type. In *Gaucher's disease* there is marked enlargement of the liver and a brownish discoloration of the skin, with a peculiar yellowish, wedge-shaped thickening of the conjunctiva, but no jaundice.

**Acquired hemolytic jaundice with splenomegaly (Hayem-Widal syndrome)** usually appears first after puberty. The patient is distinctly more anemic than jaundiced; indeed, during exacerbations the blood changes may be so marked as to suggest pernicious anemia. Nucleated red cells are frequently present when the anemia is severe, and the auto-agglutination test[4] is positive. Although the disease shows a slight tendency to recovery, it is prone to continue with periods of aggravation and regression for years. It must be differentiated from pernicious anemia, Banti's disease, and Hanot's cirrhosis of the liver. In *pernicious anemia* the spleen is rarely so large as in hemolytic jaundice, jaundice is usually absent, the resistance of the erythrocytes is increased rather than diminished, leucopenia with relative lymphocytosis is commonly present, and achylia gastrica and symptoms referable

[1] Normally hemolysis begins in salt solution of 0.45 per cent. and is complete at 0.35 per cent. In hemolytic jaundice, however it begins at 0.6 per cent., or even 0.7 per cent., and may be complete at 0.5 per cent.

[2] Surg., Gynec. and Obstet., 1917, xxv, No. 2.

[3] "The hemolytic diseases are the children, and the spleen is their mother, but the father is still unknown, and possibly there are several fathers;" Türck: Deutsch. med. Woch., 1914, xl.

[4] When 1 drop of the patient's washed red corpuscles is added to 10 drops of his own serum in a watch-glass the mixture in a few minutes deposits a distinct pellicle which does not mix with the clear serum on shaking.

to changes in the spinal cord are frequently observed. In Banti's disease hemorrhages from the gastrointestinal tract are common, if jaundice is present, which is exceptional, it is accompanied by choluria, the resistance of the erythrocytes to hypotonic salt solution is not decreased, and the number of reticulated red cells is within normal limits. In *Hanot's cirrhosis* the liver is greatly enlarged, the jaundice is accompanied by choluria, the resistance of the erythrocytes is normal or increased, the reticulated red corpuscles are not in excess, and there is no pronounced secondary anemia.

**Treatment.**—The persistent use of iron seems to have been of service in some cases of the acquired form, but the drug is useless in the congenital type. Roentgen-ray treatment has been beneficial in some cases. If the disease causes much inconvenience splenectomy should be considered, but the operation should be avoided during a crisis. Elliott and Kavanel[1] report that of 48 cases subjected to operation, death occurred in only 2. In the other 46 the symptoms virtually disappeared. Giffin,[2] of the Mayo Clinic, reports 12 cases treated by splenectomy, with 1 operative death and 1 death four months after operation. Of the 10 patients who survived the operation 9 were in excellent health at the time of the report and 1, who had had a relapse after two years, was in fairly good health, following two transfusions.

## SPLENOMEGALY WITH ANEMIA

The term "splenic anemia" was employed first by Griesinger and Gretzel[3] to designate cases of chronic enlargement of the spleen with marked anemia but without leucocytosis. Subsequent studies made it apparent that several clinical conditions of uncertain etiology were included under the term. In one group of cases, as Banti[4] first pointed out, the splenic enlargement and anemia are followed after a variable period, usually several years, by cirrhosis of the liver and ascites. To this group the name *Banti's disease* has become attached. Other conditions that have been more or less clearly differentiated from the parent group are the *acquired* and the *congenital or familial types of hemolytic jaundice*, in which there is chronic enlargement of the spleen with an acholuric jaundice, increased fragility of the red blood-corpuscles, and anemia, and also the rare disease first described by Gaucher in 1882 and which has since borne his name (*Gaucher's disease*). The clinical picture of this condition is somewhat similar to that of the earlier stages of Banti's disease, but the spleen presents, histologically, characteristic large vesicular cells (large-celled splenomegaly). The *anemia infantum pseudoleukemica of von Jaksch* is probably not an independent disease, but the infantile expression of a number of conditions seriously affecting the blood, such as Banti's disease, pernicious anemia, leukemia, the secondary anemia of rickets, syphilis, etc., the departure from the adult type being due to a difference in the reaction of the infantile hemopoietic system to the excitant. At present it is advisable to reserve the term *splenic anemia* for the early stage of the symptom-complex known as Banti's disease.

[1] Surg., Gynec. and Obstet., 1915, xxi, 26.
[2] *Loc. cit.*
[3] Berlin. klin. Woch., 1866, ii, 212.
[4] Semaine méd., Paris, 1894, xiv, 318.

## BANTI'S DISEASE

(Splenic Anemia)

**Definition.**—A chronic disease of unknown etiology, characterized by progressive enlargement of the spleen, anemia of a secondary type, a tendency to hemorrhages and also in the late stages to cirrhosis of the liver and ascites.

**Etiology.**—The cause is unknown, and there is some doubt about the disease being a definite entity. The majority of cases occur in middle life, although the disease is not uncommon in childhood. Males are affected more frequently than females. A familial incidence has occasionally been observed (Brill, Collier, Wilson). Evidences of syphilis are sometimes obtained (Chiari, Marchand, Luzzatti, Mayo), and in a few instances antisyphilitic treatment seems to have effected a cure (Schmidt, Curschmann). The nature of the process is obscure. That the enlargement of the spleen is an essential factor is shown by the fact that removal of the organ is frequently followed by complete cure. The most plausible theory is that the primary cause is an intoxication of some kind that acts on the spleen in such a way as to increase its hemolytic function. It is conceivable that the changes in the liver may be due to a secondary poison elaborated by the splenic substance.

**Morbid Anatomy.**—The spleen is greatly enlarged, frequently weighing 1 or even 2 kg. The capsule is thickened and perisplenic adhesions are often present. The splenic veins may be dilated, tortuous, and markedly sclerotic. Thrombosis of the main vessel is not uncommon. The most important change in the spleen itself is a diffuse fibrous hyperplasia with atrophy of the pulp and Malpighian bodies. The liver in many of the advanced cases presents varying degrees of atrophic cirrhosis. A moderate hyperplasia of the bone-marrow is sometimes found.

**Symptoms.**—Banti's disease is commonly divided into three stages. The important features of the first stage, which usually lasts several years, are a gradual enlargement of the spleen and after a time a moderate degree of anemia. In the second stage, which may last but a few months, the urine is scanty, high colored, and often albuminous. Digestive disturbances usually occur and not rarely the liver is somewhat enlarged. A tendency to hemorrhages, especially from the stomach or bowel, is also frequently present. In the third stage there are signs of hepatic cirrhosis with ascites, progressive anemia and emaciation, and in exceptional cases slight jaundice.

When the disease is well developed the spleen often extends below the navel and beyond the median line. It preserves its normal contour and is smooth and firm. Occasionally there is local pain in consequence of perisplenitis or infarction. The anemia becomes more pronounced as the disease progresses, although in some cases the splenic enlargement precedes it by several years. It is of the secondary type, with chloranemia, and usually, but not invariably, leucopenia. Evidences of active regeneration (nucleated red cells and reticulated red cells) are slight or entirely absent. Hemorrhages (usually from esophageal varices) occur in about 50 per cent. of the cases. A brownish or grayish pigmentation of the skin is occasionally observed. Paroxysms of slight fever may occur from time to time, but as a rule, the temperature is normal throughout. The ascites is a late phenomenon. Rarely it appears to be due to the splenomegaly itself rather than to any change in the liver.

The disease is essentially chronic and may be in evidence for years before it seriously affects the general health. A duration of ten years is not uncommon. Periodic remissions and exacerbations sometimes occur. Death

may be due to asthenia, hemorrhage, acute thrombosis of the superior mesenteric veins, or intercurrent infection.

**Diagnosis.**—Splenic enlargement being a characteristic feature, Banti's disease must be distinguished from other conditions attended by splenomegaly and pursuing a chronic course, such as chronic hemolytic jaundice, Gaucher's disease, Hanot's cirrhosis of the liver, atrophic cirrhosis of the liver, malignant disease of the spleen, chronic malaria, kala-azar, syphilitic splenomegaly, Hodgkin's disease, pernicious anemia, the leukemias, erythremia (Vaquez's disease), massive tuberculosis of the spleen, splenomegaly from obstruction of the splenic and portal veins, and chronic infective endocarditis with multiple infarcts in the spleen.

The characteristic features of *chronic hemolytic jaundice*, which is frequently congenital and familial, are more or less persistent acholuric jaundice, diminished resistence of the red cells to hypotonic salt solution, an increase in the number of reticulated red cells, and a pronounced increase in the urobilin output. Nucleated red cells may also be found in the blood if the anemia is severe, which is often the case in the acquired form. In the latter, too, the auto-agglutination test is usually positive. Hemorrhages are rare.

*In Gaucher's disease* the changes in the blood are similar to, but less marked than those in Banti's disease, the liver is considerably enlarged, a brownish discoloration of the skin with yellowish wedge-shaped thickenings of the conjunctiva is often noted, and ascites is very rare.

In *Hanot's cirrhosis of the liver* the splenomegaly is almost always much less pronounced than the hepatic enlargement, which is the primary feature, jaundice is present throughout, and leucocytosis is frequently observed. The clinical picture of advanced *atrophic cirrhosis of the liver* so closely resembles that of the later stages of Banti's disease, that differentiation may be impossible unless it is known that the patient has been addicted to the use of alcohol and that the hepatic symptoms developed prior to the splenomegaly.

*Malignant disease of the spleen* is usually suggested by the rapid course, the irregular contour of the organ, the wasting, cachexia, etc. The diagnosis of *amyloid spleen* is based on the etiologic factors, indications of amyloid change in other organs (polyuria, albuminuria, colliquative diarrhea, etc.), and the progressive weakness and emaciation.

The *splenic enlargement of chronic malaria* may be excluded by the history and the presence of the specific parasites in the blood, and that of *kala-azar* by the history of tropical residence and of periodic fever, and the detection of Leishman-Donovan bodies in the blood or in material obtained by splenic or hepatic puncture. A positive Wassermann reaction and other evidences of syphilis are the only features by which *syphilitic splenomegaly* can be distinguished from Banti's disease. Indeed, a few clinicians[1] believe that the latter is always of syphilitic origin. *Hodgkin's disease* is not likely to be mistaken for Banti's disease unless the splenic enlargement is very pronounced and the glandular swelling is confined to the mediastinal or abdominal lymph-nodes. The existence of a special splenic variety of Hodgkin's disease is doubtful. The definite blood changes in *pernicious anemia* and the *leukemias* are, as a rule, quite diagnostic. In *Vaquez's disease* there is polycythemia with chronic cyanosis and various subjective nervous symptoms. *Primary massive tuberculosis of the spleen* may simulate Banti's disease, but it is usually accompanied by considerable pain and discomfort in the splenic region and rapidly developing weakness and emaciation. In some instances, too, it is productive of polycythemia

[1] See Norris, Symmers, and Shapiro; Amer. Jour. Med. Sci., Dec., 1917.

rather than anemia. *Splenic enlargement secondary to thrombotic obstruction* of the splenic and portal veins is clinically indistinguishable from that of Banti's disease. In fact, thrombosis of the splenic vein is common accompaniment of Banti's disease. *Chronic infective endocarditis* with multiple splenic infarctions may readily be mistaken for Banti's disease if fever, petechiæ, and cutaneous erythematous nodes are absent, and leucopenia is present instead of leucocytosis. Usually, however, the cardiac murmurs of endocarditis are quite different from the hemic murmurs of Banti's disease. In endocarditis, too, the blood culture may reveal streptococcus septicemia.

**Treatment.**—If there is a suspicion of syphilis energetic antisyphilitic treatment should be instituted, although too much should not be expected from it. Iron and arsenic are virtually without effect. Indeed, splenectomy, as originally advocated by Banti, is the only measure that offers any chance of permanent benefit. If done in the first or second stage, the operation is not only attended by a comparatively low mortality (10 to 15 per cent.), but in the large majority of cases is followed by a cure or great and lasting improvement. In the third stage, with permanent changes in the liver, splenectomy is much more dangerous (mortality, 25 to 50 per cent.) and is much less likely to be of benefit, although even at this late period it has been more or less successful in some instances. A combination of splenectomy and Talma's operation has been recommended for advanced cases.

### GAUCHER'S DISEASE

**(Large-celled Splenomegaly)**

This rare disease was first described by the man whose name it bears in 1882.[1] It is frequently familial, but it is not hereditary, and it begins, as a rule, in early life. The characteristic pathologic feature is the presence in the hemopoietic organs—spleen, liver, lymph-nodes, and bone-marrow—of large vesicular cells with small, eccentrically-placed nuclei. The chief symptoms are progressive enlargement of the spleen, which may reach colossal proportions; marked enlargement of the liver succeeding that of the spleen; a brownish discoloration of the skin, with peculiar yellowish wedge-shaped thickenings of the conjunctiva on both sides of the cornea; and usually slight anemia with leucopenia. Jaundice is absent and ascites is very rare. Epistaxis and bleeding from the gums and into the skin are somewhat common in the later stages. In a few instances the diagnosis has been comfirmed by the detection of the characteristic cells in material obtained by splenic puncture. The course of the disease is chronic and for years the general health may not be seriously disturbed. Death is usually caused by some intercurrent affection. Splenectomy offers the only hope of cure, but it should not be urged unless the degree of ill-health is sufficient to justify the risk, and following the operation x-ray treatment should be employed.

## TUMORS AND CYSTS OF THE SPLEEN

**Tumors** of the spleen, whether benign or malignant, are rare. A few examples of angiomas, lymphangiomas, and fibromas are on record. Malignant growths may be primary or secondary. The former are extremely rare and almost invariably sarcomatous. Up to 1912 only 36 cases of

[1] Gaucher, E.: De l'épithelioma primitif de la rate, Thèse de Paris, 1882.

primary sarcoma of spleen had been recorded (Council[1]). Whether the cellular proliferation occurring in Gaucher's disease constitutes a neoplasm is doubtful. Even secondary malignant tumors of the spleen are by no means frequent. In 975 cases of carcinoma and sarcoma the spleen was secondarily involved in less than 5 per cent., and in many of these the invasion was by extension rather than by metastasis. *Clinically*, there may be a rapidly produced nodular enlargement of the organ, with local pain and tenderness, emaciation and cachexia.

**Cysts** of the spleen are occasionally observed. Four varieties may be recognized: Simple (serous, hemorrhagic, lymph), parasitic (echinococcus), neoformative (lymphangioma, hemiangioma), and dermoid. If large, a cyst may reveal itself by local pain and tenderness (perisplenitis), functional disturbances of adjacent organs, and the occurrence of a fluctuating mass in the left hypochondrium. The diagnosis can rarely be made with certainty. Exploratory puncture may afford valuable information, but it is by no means free from danger. Treatment is surgical, by splenectomy or partial resection.

[1] Ann. Surg., 1912, lvi, 915.

# DISEASES OF THE DUCTLESS GLANDS

## GOITER

(Simple or Non-toxic Goiter; Struma)

The term goiter is applied to nearly all enlargements of the thyroid gland except those resulting from inflammatory conditions and from new-growths other than benign adenoma. Simple goiter must be distinguished from so-called exophthalmic goiter in which the chief pathologic feature is a diffuse hyperplasia and hypertrophy of the thyroid parenchyma, with a scarcity or absence of colloid material.

**Etiology.**—Goiter occurs sporadically throughout the world; it is endemic in many countries, and occasionally under conditions of crowding, especially in goitrous localities, it becomes epidemic. In Europe endemic goiter is found particularly in the Swiss and Italian Alps and in the Pyrenees; in this country it is especially common in the region of the Great Lakes. The essential cause of the disorder is still unknown, although it is believed to be associated with drinking water. There is no unaminity of opinion, however, as to whether the impurity in the water is of an infectious nature or is of mineral origin. The disease may be congenital and apparently it is sometimes hereditary. Women are much more frequently affected than men.

**Morbid Anatomy.**—Goiter is usually bilateral, although in many cases one lobe (usually the right) is affected more than the other. Occasionally, portions of aberrant thyroid tissue at the base of the tongue, in the trachea, or even in the pleural cavity develop into tumors. Several varieties of simple goiter may be recognized, although combinations of two or more varieties are frequently observed:

1. *Colloid Goiter.*—In this, the most frequent form of goiter, the alveoli are increased in size and distended with colloid material, often to such a degree that the lining epithelium is flattened. In some cases the distention of the alveoli proceeds so far that large cavities form and then the condition is known as:

2. *Cystic Colloid Goiter.*—Hemorrhagic extravasations, calcareous infiltrations, and various degenerations, such as mucoid, hyaline and fatty, are not uncommon in goiters of this type. Colloid goiters are usually unattended by any evidences either of hyperthyroidism or of hypothyroidism, their chief manifestations being, as a rule, local.

*Adenomatous Goiter.*—This form is characterized by an endless multiplication of the acini (diffuse adenoma) or much more frequently by the presence of one or many circumscribed and encapsulated nodules, made up of numerous small alveoli, lined with cubical epithelium and separated from one another by a fairly abundant stroma. Combinations with colloid goiter are not uncommon and even cystic formation may occur. Adenomatous goiter usually develops in the second decade of life and may remain small or attain a large size. It may exist indefinitely without producing any systemic disturbance, but in many cases after a variable interval, often years, it gives rise to thyrotoxic symptoms (toxic goiter). The enlargement of the thyroid that is frequently observed in young girls about the time of puberty is

adenomatous. It is apparently compensatory in nature and associated in some way with a demand of the body for thyroxin. It is often transitory and if it produces toxic symptoms at all they are usually of mild degree.

*Fibrous Goiter.*—This term has applied to cases of colloid goiter in which the capsule of the gland is much thickened and there is an extensive hyperplasia of connective tissue between the acini, which are often more or less compressed. The goiter that is sometimes present in endemic cretinism is not uncommonly fibrous.

**Symptoms.**—Goiters vary in size from a barely perceptible swelling to a large pendulous mass weighing several pounds. As a rule, the gland is larger than the external appearances indicate, and occasionally the entire tumor is behind the sternum. To the hand, the swelling may be firm and elastic, soft and spongy, or fluctuating. It develops slowly, is not adherent to the overlying skin, moves with deglutition, and is usually painless. In the majority of cases the disfigurement is the only cause of complaint, but sometimes symptoms of hyperthyroidism or of hypothyroidism supervene, and not rarely more or less disturbance arises from the pressure of the tumor on contiguous structures. Dysphagia is present in some cases, but dyspnea, stridor, and cough from pressure on the trachea are much more common. Circulatory disturbances may also occur and are usually of toxic origin (thyrotoxicosis), although occasionally mechanical interference with the lesser circulation may be a factor.

The *diagnosis* of simple goiter is usually easy, the condition being readily distinguished, as a rule, from exophthalmic goiter (see p. 852) and congenital cysts. Malignant growths and tubercle of the thyroid may be difficult to exclude, but are comparatively rare.

**Treatment.**—In goitrous regions it is advisable for persons who become affected to change their residence. If this is impracticable they should drink only boiled water. In early cases applications of iodin in the form of the tincture or of an ointment of cadmium iodid—20 grains to the ounce (1.3 gm. to 30.0 gm.)—and the use of iodids or thyroid extract internally is often of service, although in persons more than 40 there is some danger of such medication transforming an atoxic goiter into a toxic one. Levin[1] has shown that 30 grains (2.0 gm.) of sodium iodid, taken in doses of 3 grains (0.2 gm.) for 10 days twice yearly, is not only effective in reducing thyroid enlargements but in preventing them. X-rays have also been used with some success. Large and growing goiters, and especially those producing marked toxic symptoms, should be treated surgically.

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## EXOPHTHALMIC GOITER

**(Parry's Disease; Graves' Disease; Basedow's Disease)**

**Definition.**—Exophthalmic goiter is a relatively common disease, characterized by tachycardia, exophthalmos, enlargement of the thyroid gland, fine muscular tremors, an excitable condition of the nervous system, and evidences of increased basal metabolism.

Incomplete forms of the disease (formes frustes) without exophthalmos and with only slight enlargement of the thyroid are by no means rare, but many of these are now regarded as examples of pure hyperthyroidism, or so-called toxic goiter (see p. 854.)

[1] Arch. Int. Med., April 15, 1921.

**History.**—Although the condition was recognized by Parry in 1815, the first full descriptions of it were given by Graves in 1835 and by Basedow in 1840. To Möbius belongs the credit of associating the disease with increased activity of the thyroid gland.

**Etiology.**—The disease is much more frequent in females than in males, in the proportion of 5 or 6 to 1. It occurs chiefly between the ages of 15 and 45, and is decidedly uncommon in children and in persons over 60. Periods of physiologic stress, such as puberty and the menopause, afford a special predisposition. That pregnancy has some influence has long been recognized. Heredity plays a certain rôle, but not an important one. Instances are not rare, however, in which the disease has attacked several members of one family or has occurred in successive generations.

Symptoms of hyperthyroidism are often consequent upon simple goiter and sometimes develop in the course of other affections of the thyroid, such as acute inflammation, carcinoma and tubercle, but true exophthalmic goiter has rarely this origin. In many cases no exciting cause can be demonstrated but frequently a history of profound emotional disturbance (fright, anxiety, grief, worry, etc.) or of overwork is obtainable. The acute infections, especially influenza, are also antecedents of the disease in a significant number of cases.

**Pathogenesis.**—The conspicuous features of exophthalmic goiter undoubtedly depend upon excessive activity of the thyroid gland. In favor of this view are the observations that the administration of large doses of thyroid extract to a normal person is capable of producing symptoms closely resembling those of exophthalmic goiter, that hyperplasia of the thyroid is almost invariably found in association with the disease, and that the affection is often cured by the removal of a portion of the thyroid. The whole symptom-complex, however, cannot be attributed merely to hyperthyroidism. Possibly the thyroid secretion is perverted as well as increased. The influence of the nervous system must also be considered, otherwise it would be difficult to explain why exophthalmic goiter so frequently follows in the wake of psychic shock or emotional disturbances or why marked improvement in the symptoms or even cure of the disease not rarely results from physiologic rest alone.

It has been shown that the thyroid is under the control of the sympathetic nervous system (cervical sympathetic), and it is not improbable that in certain individuals emotional stress, overwork, acute infections, etc. may so lower the neuron threshold interposed between the central nervous system and the thyroid that the latter is exposed to excessive stimulation. By fusing in the cat the anterior root of the right phrenic nerve with the right cervical sympathetic strand, thus permitting a volley of impulses to reach the superior cervical ganglion every time the animal breathed, Cannon, Binger, and Fitz,[1] were able to produce an almost typical picture of exophthalmic goiter. L. B. Wilson[2] has shown that definite changes occur in the cervical sympathetic ganglia in exophthalmic goiter and that histologic pictures within the ganglia and in the thyroid resembling those found in exophthalmic goiter in man can be produced by electric stimulation of the ganglia or the injection of bacteria into them.

Once the symptom-complex of Graves' disease is produced the development of a so-called vicious circle may serve to perpetuate it. Thus, excessive sympathetic stimulation increases the output of thyroid secretion, and the effect of this in turn is to increase still further the excitability of the

[1] Amer. Jour. of Physiolog., Mar., 1915.
[2] Amer. Jour. Med. Sci., Dec., 1916; Oct., 1918.

nervous system. Von Cyon's observation that an excess of thyroid secretion directly increases the blood flow through the thyroid, if correct, would indicate the operation of another vicious circle. Again, over activity of the thyroid seems to increase suprarenal activity, and this effect is likely to result in abnormal sympathetic stimulation. However the status of exophthalmic goiter is produced and maintained, normal functioning is usually restored when the influence of the thyroid is removed.

Some of the symptoms of exophthalmic goiter are due to physical changes in the thyroid itself (pulsating goiter), others apparently owe their origin to increased sympathetic stimulation (tachycardia, exophthalmos), and others still to augmented metabolism (muscular weakness and emaciation).

The active constituent of the thyroid appears to be the crystalline compound containing 65 per cent. of iodin that was separated by Kendall[1] in 1915 and named thyroxin. This body, which is of the nature of a hormone, determines the rate of transformation of energy in the organism. The tissues of the body exclusive of the thyroid normally contain about 14 mg., the average daily exhaustion of it being between 0.5–1.0 mg. A daily oral dose of 1.6 mg. will usually maintain thyroidless individuals in a normal condition (Plummer), and the administration of more than 1 mg. daily to a normal person is commonly productive of hyperthyroidism. It seems to be the function of the so-called colloid in the acini of the thyroid to store the iodin required for elaboration of thyroxin. In exophthalmic goiter the amount of colloid is much reduced and the per cent. of iodin is low, the blood gaining in this substance at the expense of the gland.

**Morbid Anatomy.**—The thyroid is nearly always more or less enlarged, is sometimes nodular, and may be firm or soft. The vessels are numerous and distended. The characteristic microscopic change is a diffuse hypertrophy and hyperplasia of the parenchyma. The alveoli are no longer uniform in size and shape, and the colloid matter that normally fills them is usually scanty or entirely absent, its place being taken by a small amount of mucoid fluid that stains poorly. The epithelium, instead of being low and cuboidal, is high and columnar and is so increased in amount that it is thrown into folds, presenting a distinctly papillary arrangement. Lymphoid nodules are frequently found throughout the gland, the bloodvessels are increased, and the connective tissue stroma usually shows evidences of proliferation, especially in long standing cases.

With improvement in the symptoms the colloid returns to the acini and the proliferated parenchyma undergoes retrograde changes (degeneration and exfoliation). When myxedematous features supervene, which is occasionally the case, the involutional process advances until the epithelium becomes distinctly atrophic. The changes, however, are not confined to the thyroid. The thymus gland is usually enlarged; the lymph-nodes, especially those in the neck, are often considerably swollen; the cells of the superior cervical sympathetic ganglia show degenerative changes; and in advanced cases the orbital fat is increased, the heart is enlarged and degenerated, and the muscles are pale and fatty.

**Symptoms.**—The *onset* is, as a rule, insidious, the characteristic symptoms appearing gradually one after another. Subjective cardiac disturbances, especially palpitation, or general nervousness and ready fatigability are usually the first obtrusive features. Only in a small proportion of cases is thyroid enlargement or exophthalmos the first sign to attract attention. A sudden onset is much less common, and what appears to be such is often only an exacerbation in the course of a comparatively latent hyperthyroidism.



[1] Jour. Amer. Med. Assoc., 1915, lxiv, 2042.

*The Nervous System.*—Restlessness, mental excitability, irritability of temper and rapidly alternating moods are fairly constant features. In addition, there is often a decided lack of physical endurance, with the usual phenomena of fatigue, hence in the early stages the condition is sometimes mistaken for primary neurasthemia. Occasionally, in the more severe forms there are hallucinations or delusions, and rarely actual mania or melancholia supervenes. Even more characteristic than the psychic symptoms is a fine vibratory tremor (8 to 10 oscillations per second). This is especially marked in the fingers and is best seen when the hands are extended with the fingers separated. The most common sensory disturbance is a subjective feeling of heat independent of fever or the external temperature. Headache, neuralgic pains in various parts of the body, painful muscular cramps, itching of the skin, and other paresthesias are sometimes observed.

*The Circulatory System.*—Persistent tachycardia is one of the most important signs and is probably never absent. The pulse-rate is virtually always over 90 and may exceed 200. With the increased frequency of the pulse there is, as a rule, paroxysmal palpitation, although this symptom may be absent in slight or early cases. The rhythm of the pulse is often regular throughout, but in advanced cases arhythmia, the result of extra-systoles, auricular fibrillation or even auricular flutter, is by no means infrequent. Throbbing of the carotids and of the abdominal aorta is often a conspicuous feature. As the disease progresses signs of cardiac hypertrophy or dilatation commonly appear. At first the heart sounds are unusually loud and distinct, the first sound at the apex being especially accentuated; later the sounds become less intense and clear, and in many cases a systolic murmur develops at the apex. The blood pressure changes are analogus to those in aortic regurgitation (increased systolic output with low peripheral resistance), the maximal arterial pressure being usually high, the minimal low or normal, and the pulse-pressure, therefore, increased. The Corrigan pulse and the capillary pulse are also occasionally observed. With increasing weakness of the heart, ascending edema frequently supervenes. In a few instances there is precordial pain of an anginoid character.

*The Blood.*—The erythrocyte count is, as a rule, within normal limits, except in the later stages of the disease when a greater or less degree of secondary anemia may develop. The leucocyte count, in the majority of cases, even at an early stage, shows an increase in the lymphocytes, both relative and absolute, with a corresponding decrease in the polymorphonuclear neutrophiles.

*The Thyroid Gland.*—Some enlargement of the thyroid is almost always discernible, and in not a few instances the swelling attains a considerable size. Occasionally, the swelling is so slight that it is scarcely perceptible and rarely it is absent altogether, the entire goiter being intrathoracic. The whole gland is, as a rule, involved although one lobe may be larger than the other. There is no relation between the size of the thyroid and the severity of the symptoms. Variations in the size of the gland occur from time to time, a temporary increase frequently being noted after unusual excitement or exertion, and during menstruation. The arteries of the enlarged gland often pulsate strongly and in the majority of cases palpation reveals a distinct thrill, and auscultation a loud systolic murmur or continuous bruit. The goiter itself is usually painless and unless very large is not likely to cause pressure symptoms.

*The Eyes.*—When well marked, the exophthalmos is the most impressive feature of the disease. It may be slight, however, and sometimes it is absent altogether. It usually appears within a few months or a year of the onset

and may develop gradually or abruptly. In some instances it is unequal on the two sides, and rarely it is unilateral. When the protrusion of the eyeballs is pronounced the eyelids cannot be closed at all. The cause of the exophthalmos is not definitely known, although by many it is thought to be the result of a spastic condition of Landström's muscle,[1] which is innervated by the sympathetic. The excess of retro-bulbar fat that is found postmortem in certain cases is an effect of the exophthalmos and not its cause. Retraction of the upper eye-lid with widening of the intra-palpebral fissure, (Dalrymple's sign) is another important feature. It sometimes precedes the development of the exophthalmos and may occur when the latter is absent throughout. This sign, which probably depends upon stimulation of the unstriated muscle-fibers of Müller in both eye-lids, allows some of the sclera to be seen above and below the edge of the cornea when the eye is directed straight to the front in the horizontal plane, and together with the exophthalmos gives to the patient a wild staring look, sometimes amounting to an expression of terror ("crystallized terror"—Möbius). Von Graefe's sign, or lagging of the upper lid when the eye is turned very slowly from above downward, is also important, although it is not always present and is not pathognomonic of Graves' disease. Somewhat less constant is Stellwag's sign, which consists of infrequency in winking. Difficulty in converging the two eyes when looking at near objects, as described by Malbius, is sometimes observed. It is probably due to insufficiency of the overstretched internal recti muscles. Swelling of the lids is not uncommon. Among rarer eye-symptoms may be mentioned pigmentation of the upper lid (Jellinck and Rosin), jerking of the globe at the instant of changing the movement of the eyes from abduction to adduction (Wilder), epiphora, or an overflow of tears, tremor of the eye-lids, pulsation of the retinal artery (Becker), a bruit over the eye-ball (Snellen), and paralysis of one or more of the external ocular muscles (Stellwag, Jendrassik). Owing to increased exposure of the conjunctiva, inflammation of this membrane frequently develops and occasionally ulceration of the cornea occurs.

*The Gastro-intestinal Tract.*—While the appetite is usually good and may be voracious, it occasionally fails or becomes perverted. Vomiting is somewhat common in severe and acute cases, and not rarely precedes a fatal termination. Gastric achylia is observed in many cases. The most frequent disturbance of the alimentary canal, however, is diarrhea, which may be periodic or persistent. It has been ascribed by some authors to irritation of the vagus and by others to achylia.

*The Skin.*—Of cutaneous symptoms, free perspiration, especially of the hands and feet, is the most common. Occasionally the hyperidrosis takes the form of night-sweats. Pigmentation of the skin and signs of vaso-motor instability—erythema, urticaria, localized evanescent edema, etc.—are observed in many instances. The tendency to pruritus has already been mentioned. Falling of the hair is sometimes an annoying feature.

*The Urogenital Symptoms.*—The urine is, as a rule, normal in amount and free from albumin and sugar, but sometimes there is glycosuria or transient albuminuria. Polyuria has also been observed. Menstrual irregularities are common.

*Metabolism.*—As a result of the presence of an excess of thyroxin in the body the basal metabolic rate is almost always increased, the figures ranging from + 15 to + 50 in the milder cases to over + 75 in the severe cases. Basal metabolism is measurable in terms of heat production and this may

[1] Landström's muscle is a cylinder of plain muscle arising from the septum orbitale anteriorly and inserted just posterior to the equator of the eyeball.

be determined clinically by indirect calorimetry, using the portable respiration apparatus devised by Benedict and estimating the quantity of oxygen utilized while the subject is at complete physical and mental rest and in the postabsorptive state, that is twelve hours or more after taking food. From the readings of oxygen consumption the calories produced per square meter of body surface per hour may be calculated and compared with the standard of average values, based on age and sex. A variation of 15 per cent. from the average is considered within the normal limit. Of course, every patient with a basal metabolism above + 15 is not suffering from hyperthyroidism. High figures are also observed in leukemia, pernicious anemia, and various febrile conditions.

The oxidation of carbohydrates is often disturbed in exophthalmic goiter, and even in mild cases alimentary hyperglycemia and glycosuria are not uncommon. Even when patients are maintaining their weight and storing nitrogen, creatinuria is frequently observed. The body-temperature is usually normal; occasionally, however, the elimination of heat does not keep pace with the increased production and slight fever develops. A more important effect of the increased metabolism is the wasting of the body, which occurs in all acute and severe cases. A decrease of 25 or 30 pounds within a few months is not uncommon. Exceptionally, in mild cases the opposite effect is noted and the patient's weight increasing somewhat instead of decreasing.

In a few instances exophthalmic goiter has been associated with acromegaly (Lorand)[1] or with Addison's disease (Etinne and Richard[2]). Occasionally, as a result of secondary atrophy of the thyroid parenchyma, the symptoms of exophthalmic goiter are followed by those of myxedema.

**Diagnosis.**—When well developed exophthalmic goiter is readily recognized, but the diagnosis of early cases and of incomplete forms of the disease is sometimes difficult. Persistent tachycardia should always arouse suspicion and every patient presenting it should be carefully examined for thyroid enlargement, exophthalmos and tremor. In doubtful cases an augmented metabolic rate points strongly to hyperthyroidism. A definite reaction with Goetsch's test, which is based upon the increased constitutional sensitiveness of the thyrotoxic patient to epinephrin, is also valuable corroborative evidence, although it is not always obtainable and is not pathognomonic of Graves' disease. The test consists in the injection ½ mil of a 1:1000 adrenalin solution subcutaneously after the patient has been at complete physical and mental rest for at least 24 hours. In so-called positive reactions there is an early rise in the systolic blood pressure and a fall in the diastolic blood pressure, together with an increase in the pulse-rate from 10 to 50 per minute, and an exaggeration of the nervous symptoms. In the course of 30 or 35 minutes there is a moderate fall in the pulse-rate and blood pressure, followed by a characteristic secondary rise and then a second fall to normal in about one and a half hours.

In the differential diagnosis of Graves' disease *simple goiter* and *exophthalmos due to retrobulbar growths, sinus thrombosis or abscess, aneurysm* or *hydrocephalus* can usually be excluded without difficulty.

**Course and Prognosis.**—The duration of exophthalmic goiter varies greatly. As a rule, however, the disease pursues a chronic course extending over many years, and usually marked by definite remissions and exacerbations, or so-called crises. Each crisis leaves the patient a little less virile than he was before and increases the damage to the heart and other organs.

[1] Trans. xiv Internat., Cong. Madrid (1903); Sect. Neurol., 490.
[2] Bull de la Soc. mèd. des Hôp., 1918, xliii, 1196.

The acute form of Graves' disease which is comparatively rare, may end fatally within a few weeks, although if mild it may become chronic or soon terminate in recovery. Probably 75 per cent. of all patients with exophthalmic goiter are cured or are much improved under appropriate therapy and not more than 10 per cent. die as a result of the disease itself. Indeed, in mild cases spontaneous recovery is not uncommon. Surgical measures, on the whole, yield better results than medical treatment. In cases terminating fatally death may be due to cardiac insufficiency, to exhaustion from vomiting or diarrhea, or to intercurrent infection. The mortality is proportionately greater in men than in women. In individual cases the rapidity of the pulse, the rate of metabolism and the degree of emaciation are the best indices of the intensity of the intoxication.

Pregnancy has in many cases an unfavorable influence upon the course of the disease, although occasionally it may be followed by pronounced improvement or even by actual recovery. Relapse is by no means uncommon and may occur years after recovery.

**Treatment.**—The treatment aims at lessening the excitability of the nervous system and diminishing the output of the thyroid secretion. Rest of body and mind is absolutely essential. Even in mild cases the rule should be two or three weeks of complete rest in bed, and after this period at least ten hours of rest at night with an additional hour or two during the day. In severe cases and during acute exacerbations of less severe cases the period of complete rest should be from four to six weeks or even longer. As much time as possible should be spent in the open air. Freedom from worry and excitement of all kinds is no less an important element of the treatment than exemption from physical exertion. The rest is effective not only in restoring nervous control but also in securing a marked reduction in metabolism. Psychotherapy and suggestion are not without influence; indeed, it is likely that good effects have sometimes been ascribed to remedies that in reality were due not to the remedies themselves but to a powerful mental impression created in administering them. The diet should be abundant and nutritious, but at the same time plain and unstimulating and restricted somewhat in respect of meats. Highly seasoned dishes, tea, coffee and alcohol are, as a rule, inadmissible. If there is much loss of weight it is usually advisable to give milk between meals or on retiring. When the patient is able to be up and about a change of scene and air often proves beneficial. High altitudes should be avoided if cardiac weakness is pronounced and no place should be chosen in which the patient cannot secure good food and mental tranquility. Sea-bathing must be forbidden. Massage and general hydrotherapeutic measures, judiciously employed, may be of service. It is doubtful, however, whether the various forms of electrotherapy have more than a suggestive influence, although stabile galvanism of the cervical sympathetic has had the approval of many clinicians of large experience. The application of x-rays to the thyroid and thymus glands has in some cases proved to be of much value.

Many drugs have been highly praised from time to time, but none appears to have any influence on the fundamental process. Iron and arsenic are useful in anemic subjects. If nervous excitability and restlessness are pronounced potassium or sodium bromid, in doses of 20 or 30 grains (1.3–2.0 gm.) at bedtime, may be given with advantage. Tachycardia and palpitation are best treated by rest and the application of an ice-bag to the precordium. Belladonna given to the point of tolerance is sometimes of service, but the manner of its action is not known. Digitalis may be useful if there are evidences of cardiac dilatation, otherwise it is likely to fail.

Laxative remedies are often beneficial and it is probable that sodium phosphate, which in doses of 15 to 20 grains (1.0–1.3 gm.) three times a day, has given good results in the hands of some observers, owes its virtues to its action on the bowels. Diarrhea, which is often refractory, is best treated, as a rule, by rest in bed, liquid diet, and the administration of bismuth subcarbonate and tannalbin. In some cases hydrochloric acid by relieving achylia acts well. Persistent vomiting may require the use of morphin hypodermically. The employment of special antitoxic and cytolytic preparations (serum of thyroidectomized animals, milk of thyroidectomized goats, cytolytic serum of Beebe and Rogers, and etc.) has proved disappointing. Thymus extract is useless and thyroid extract and iodids are, as a rule, harmful.

While many patients can be cured or much benefited by well-directed medical measures, surgical intervention offers by far the greater chance of success, and for this reason is to be recommended after medical treatment has been given a fair trial or at once if the patient's circumstances are such as to render impracticable a prolonged period of rest. Operation should not be done during acute exacerbations or crises or in cases far advanced with extensive degeneration of the cardiac muscle. Auricular fibrillation is not in itself a contraindication to surgical intervention, although it adds, of course, considerably to the danger. As regards the form of operation each case presents its own problem as to whether it should be treated by boiling water injections, by ligation of one or more of the thyroid arteries, or by partial thyroidectomy. In skillful hands the mortality of thyroidectomy is at present not above 2 or 3 per cent. Crile[1] under a plan of treatment that included the adoption of nitrous oxid-oxygen, anesthesia and local anesthesia, the multiple stage operation, and the exclusion of the psychic factor, had but 2 deaths (1.1 per cent.) in a series of 181 consecutive thyroidectomies. After operation medical supervision is always necessary for several years at least.

## SECONDARY HYPERTHYROIDISM

**(Toxic adenomatous Goiter; Incomplete exophthalmic goiter)**

**Definition.**—These terms are applied to a symptom-complex supervening after a variable interval upon benign goiter, apparently due solely to excessive thyroid secretion, and comprising tachycardia, nervousness, an increased basal metabolic rate with loss of strength and weight, and eventually the usual phenomena of cardiac insufficiency.

**Etiology.**—The underlying causes are those that favor the occurrence of benign goiter. Women are much more frequently affected than men. The thyrotoxic symptoms develop most frequently in middle life, or, according to Plummer, on an average of fourteen and one-half years after the goiter is first noticed. Not infrequently over-exertion, profound emotional disturbance, or child-bearing seems to stand in etiologic relation to the symptoms. Focal infection, particularly in the tonsils, may also play a certain rôle in transforming a benign into a toxic state.

**Morbid Anatomy.**—The goiter, which has often existed from adolescence, is usually of an adenomatous nature, although areas of hypertrophy of the aveolar epithelium and an increase of intra-alveolar colloid may also be present. The adenomatous tissue may be encapsulated or diffuse. Cystic goiter rarely becomes toxic. Both tuberculosis and carcinoma of the thyroid may also be associated with hyperthyroidism.

[1] Surg., Gynec. and Obstet., Jan., 1919.

The histologic changes in the heart, which are believed to be the result of the action of the thyroxin on the nervous mechanism of the organ or on the myocardium itself, include fatty degeneration and focal or diffuse necrosis of the muscle cells, with interstitial lesions consisting of round-cell infiltration or areas of fibrosis.

**Symptoms.**—The onset is usually gradual, but it may be sudden. The symptoms, which present all grades of severity, resemble more or less closely those of exophthalmic goiter; indeed, transitional forms are frequently observed. Both conditions have in common enlargement of the thyroid, tachycardia, nervous instability, and an increased metabolic rate with loss of weight and strength. In pure hypertyroidism, however, exophthalmos is rare, although a staring expression is somewhat common; thrill and bruit over the thyroid are observed in but a small proportion of cases; irregularity of pulse develops earlier than in exophthalmic goiter, and typical crises are exceptional. The thyroid enlargement varies considerably in degree. The gland may be so small as hardly to be discernible or it may be of enormous size. Occasionally, it projects into the chest as a substernal goiter. Irregularity of the surface is seen more frequently than in Graves' disease.

**Diagnosis.**—Except in mild forms of the disease the diagnosis is not difficult. Not infrequently, however, toxic goiter is confused with *chronic myocardial disease* arising from other causes. Cases of cardiac insufficiency with tachycardia, but without signs of arteriosclerosis or of valvular lesions, should be carefully examined for thyroid enlargement, tremors, the Goetsch reaction, and, if necessary, increased basal metabolic rate. In mild cases the resemblance to primary *neurasthenia* and so-called *irritable heart* may be close, but in neither of these conditions is the Goetsch sign likely to be positive or the metabolic rate to be increased.

**Prognosis.**—This varies with the severity of the intoxication. The disease usually pursues a protracted course extending over many years. The large majority of cases are completely cured or are much benefited by appropriate treatment.

**Treatment.**—The medical treatment is that of exophthalmic goiter. Local sources of infection should be sought for and, if possible, removed. Prolonged rest and x-ray treatment are valuable and sometimes results in a permanent cure. Surgical intervention is always indicated when well-directed medical treatment fails to produce any definite or lasting improvement. As a rule, the operation should be directed at once to removal of the tumor. Preliminary ligation is rarely of benefit. The relief afforded by surgical treatment occurs earlier and is more complete in toxic goiter than in exophthalmic goiter. Even after the occurrence of auricular fibrillation marked improvement is sometimes noted.

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## MYXEDEMA; CRETINISM; HYPOTHYROIDISM; ATHYROIDISM

Three conditions arising from deficiency of the thyroid secretion are included under the general term myxedema: (1) Cretinism—congenital or acquired myxedema of infants and children; (2) spontaneous myxedema of adults; (3) postoperative myxedema.

**History.**—In 1873 Sir William Gull first described the disease which in 1877 William Ord named myxedema. Sporadic cretinism had already been described by Hilton Fagge (1871). Reverdin in 1883 and Kocher in 1884 pointed out the resemblance between myxedema and the group of symptoms

which follow total thyroidectomy, Kocher applying to the latter the name "cachexia strumipriva." A little later Sir Felix Semon suggested that the two conditions were closely related and that both were due to a loss of function of the thyroid gland. In 1890 Victor Horsley advocated thyroid grafting for the cure of myxedema, Schiff having previously demonstrated that such a procedure in dogs would prevent the ill effects of thyroidectomy. In 1891, George Murray successfully employed subcutaneous injections of a glycerin extract of sheep's thyroid in the treatment of myxedema, and in the following year Fox, Mackenzie and Howitz found that thyroid extract by the mouth was equally efficacious.

**Cretinism.**[1]—This is a chronic condition, congenital or developing before puberty, characterized by arrested physical and mental development, with dystrophy of the bones and soft parts. It prevails extensively in regions in which goiter is endemic, and sporadic cases occur in all countries. In the endemic form one or both parents may be goitrous, and in many cases the patient's thyroid is enlarged. The etiology of the sporadic form is unknown. Goiter, however, is unusual, the thyroid as a rule, being absent, undeveloped, or atrophied. Not rarely the atrophy has followed one of the specific fevers, an acute thyroiditis probably having been responsible for it.[2] Whether the thyroid is large or small, the essential lesion in cretinism is absence or deficiency of the thyroid parenchyma. The thymus often persists and in some cases there is enlargement of the hypophysis.

*Symptoms.*—Evidences of arrested development usually become apparent about the end of the first year, although in some cases nothing abnormal is observed until the child is several years old (juvenile form). When the condition is well developed it may be recognized at a glance. The body is dwarfed and misshapen. The head is large and disproportionately broad. The hair is coarse, dry and scanty. The forehead is low and usually wrinkled. The eyes are wide apart and the eye-lids are swollen and drooping. The nose is flattened and stumpy. The lips are thick and the mouth is usually open, allowing the tongue, which is large and fleshy, to protrude and the saliva to escape. The complexion is pale and waxy and the expression is stolid. The chest is comparatively small, the abdomen is large and protuberant, and an umbilical hernia is frequently present. The limbs are short, the legs are usually bowed, the hands and feet are broad and podgy. The skin is dry and often apparently edematous, although it does not pit on pressure. Soft flabby swellings are often seen about the clavicles. The teeth are late in appearing and often become carious. The sexual organs remain diminutive and hair does not appear over the pubes or in the axilla. With the exception of sight, the special senses are dull. The voice is harsh, and the gait, if the patient is able to walk at all, is waddling and clumsy. The mental condition is that of idiocy or imbecility. In many cases speech is never acquired or is limited to a few monosylables. The temperature is subnormal, movements of the body are slow, and basal metabolism is much reduced. In untreated cases prolongation of life beyond the thirtieth year is exceptional and in many instances death (usually from intercurrent disease) occurs in childhood.

In the juvenile form of cretinism the mental and physical changes vary with the age of the patient at the time he was attacked, both being less pronounced, however, than in infantile cases. The nearer the onset to puberty, the closer is the resemblance of the symptoms to those of spontaneous myx-

[1] The origin of the word "cretin" is obscure, some deriving it from *Chrètien*, Christian; others from *creta*, chalk; and others still from *cret* (Romanic), dwarf.

[2] In the disease affecting infants in Brazil, known as opilaçao, infection of the thyroid by a protozoön parasite proceeds to goiter, and, if the patient survives, to cretinism.

edema of adults. Rudimentary forms of cretinism are not uncommon and are likely to escape recognition. A cessation of body growth, especially if associated with a dry, thick skin, scanty hair and tardy development of the secondary sexual characteristics, should arouse suspicion. In the diagnosis of cretinism other forms of dwarfism are, as a rule, readily excluded. *Achondroplasia* may be distinguished by marked shortening of the long bones, enlargement of the joints, a normal mental condition, well developed musculature and sexual organs, and an absence of changes in the skin and its appendages. In *Mongolian idiocy* the forehead is smooth, the eyes are obliquely placed, the features are mobile, the expression is vivacious, the movements are active, and there is no thickening of the subcutaneous tissues. Ateleiosis, progeria and other forms of infantilism can not be mistaken for cretinism. In any doubtful case a low basal metabolic rate would be strongly suggestive of cretinism.

**Myxedema of Adults.**—This is a condition developing spontaneously as a result of insufficient thyroid secretion and characterized by physical weakness, mental deterioration, peculiar changes in the skin and evidences of reduced basal metabolism. It is the antithesis of hyperthyroidism. The disease develops most frequently between 30 and 50 and women are very much more prone to it than men. A familial disposition to it is sometimes observed. Well developed cases are somewhat uncommon in America. The exciting cause is unknown. In some instances the disease seems to have been induced by an acute infection, and occasionally it has followed recovery from exophthalmic goitre. In almost all cases the thyroid gland is much reduced in size, but it may be enlarged; in either case the essential changes are a loss of secreting structure and an excess of colloid. Enlargement of the thymus and hypophysis is sometimes observed. The subcutaneous deposits peculiar to the disease are made up largely of fat and a semifluid material which is said to be of a mucoid character, hence the name *myxedema*.

*Symptoms.*—The first symptoms to attract attention are usually those of neurasthenia and an increase in the bulk and weight of the body. The appearance of the patient gradually changes and in the course of time becomes characteristic. When the disease is well developed the features are broad and coarse, the eye-lids are puffy and translucent, and owing to narrowing of the palpebral fissure, there is elevation of the brow and wrinkling of the forehead. The lips, nose and tongue are thick. The cheeks, in contrast to the surrounding skin which is sallow and waxy, are often slightly flushed. The skin is dry, harsh, thickened and apparently edematous, although it does not pit on pressure (so-called solid edema). Localized swellings of a dough-like consistency also appear in various parts, especially above the clavicles. The hair is dry and brittle, and eventually becomes sparse or is entirely lost. Similarly the teeth fall out and the gums recede. The fingers are broad, and relatively short ("spade-like"), and the nails are brittle and ridged. Muscular movements are slow and clumsy and readily produce fatigue, the gait is lumbering, the voice is hoarse, speech is deliberate and monotonous, the acuity of the special senses is impaired, and perceptions are tardy. The mental condition at first is one of apathy and torpor, with slowness of thought, weakness of memory, and somnolence, but in the later stages there is often well-marked dementia with hallucinations or delusions, and occasionally actual insanity in the form of melancholia or mania supervenes. Chilliness is frequently complained of and in the majority of cases the temperature of the body is actually lowered. Neuralgic pains in various parts of the body and an occasional "giving way" of the legs are fairly constant symptoms. The pulse is usually slow and weak, but it may

be somewhat frequent. As in other cachexias, signs of cardiac insufficiency may develop in long-standing cases. Dyspnea on exertion is not unusual even in the early stages. Hemorrhages from the mucous surfaces sometimes occur. Menstrual disturbances, usually amenorrhea, but occasionally menorrhagia, are the rule. Pregnancy rarely occurs in well-developed cases. Albuminuria is frequently observed and there may be glycosuria, although, as a rule, tolerance for sugar is increased. As evidence of restricted metabolism, the output of nitrogen in the urine is greatly decreased and gaseous interchange is similarly on a lower level. According to the severity of the case the rate of basal metabolism ranges from −15 to −40.

In the absence of specific therapy, the course of myxedema is usually slow but progressive, the average duration being about 7 or 8 years. Death is generally due to some intercurrent affection.

The diagnosis is not difficult, except in the early stages and in rudimentary forms of the disease (*formes frustes*). The latter are by no means uncommon. The association of lassitude, somnolence, chilliness and other subjective sensations, with dryness of the skin and some loss of hair, should at least suggest the possibility of mild hypothyroidism. It is well to remember, too, that thyroidal insufficiency is sometimes responsible also for enuresis in children who are mentally backward, for amenorrhea in poorly developed girls, and for otherwise unaccountable sterility in stout women of the child-bearing age. In doubtful cases a determination of the basal metabolism will be of great help.

**Postoperative Myxedema.**—Since the abandonment of total thyroidectomy postoperative myxedema has become rare. The symptoms are very similar to those of spontaneous myxedema and appear in from a few weeks to several months after the operation.

**Treatment.**—As patients with myxedema are very susceptible to low temperatures, they should be warmly clad and protected from cold. Residence during the winter in a warm sunny climate is desirable. Warm baths are beneficial. It is important to keep the bowels regular. The essential element of treatment, however, is the more or less continuous administration throughout life of an extract of animal thyroid glands or of the thyroid hormone, thyroxin. The implantation of thyroid tissue has rarely, if ever, been successful. The most suitable dose of thyroid extract must be determined by trial in each case. It is best to begin with a small dose—2 grains (0.13 gm.) of the dried gland a day—and to increase the amount every two or three days until the symptoms begin to disappear. Usually the maximum dose of 10 to 15 grains (0.6–1.0 gm.) daily may be reached within a fortnight, and during this period if the patient shows any indications of cardiac or arterial degeneration, it is advisable for him to remain in bed. Once the full therapeutic effect of the drug has been secured, it may be maintained by smaller doses, often 5 grains (0.3 gm.) once a day, or even every second or third day, being sufficient for the purpose. Larger doses are required in winter than in summer. In all cases the dosage must be carefully supervised, as alarming symptoms sometimes develop suddenly. Dyspnea, tachycardia, vomiting or purging, marked prostration, or anginoid pains should lead to the immediate suspension of the treatment for the time. According to Plummer[1] there are approximately 10 mg. of thyroxin in 150 grams of desiccated thyroid, and a daily oral dose of 1.6 mg. of thyroxin will hold the basal metabolism of most thyroidless individuals within normal limits. As a rule, if thyroid medication is instituted early, before the occurrence of serious degenerative changes in the vascular system and kid-

[1] Jour. Amer. Med. Assoc., July 23, 1921.

neys, the symptoms entirely disappear and the patient remains well as long as the treatment is continued.

In cretinism, also, marvellous results are frequently achieved by thyroid medication, especially if it is begun early. In many cases, however, mental improvement, though marked, does not keep pace with bodily growth, and a complete cure is somewhat exceptional. Indeed, in severe endemic cretinism the patient, despite specific treatment, not rarely remains wholly idiotic.

## ACUTE THYROIDITIS

Acute inflammation of the thyroid gland may be simple or suppurative, the former ending in resolution, the latter in abscess. It may occur in a previously healthy gland, but more frequently it is preceded by goiter. Like other affections of the thyroid, it is more common in women than in men. The causative factor is not always apparent, although, as a rule, the inflammation accompanies or follows some infectious disease, such as typhoid fever, rheumatism, septicemia, influenza, acute syphilis, etc. Of 73 cases collected by Walther[1] 40 were associated with typhoid fever. French writers have reported an epidemic form among soldiers. In Brazil a variety of trypanosomiasis caused by the *Schizotrypanum cruzi* (Chagas) is accompanied by acute thyroiditis. Occasionally the disease has resulted from the administration of iodids (Kocher, Goudorow, Schültz) and rarely it has been excited by traumatism.

The chief **symptoms** are pain in the neck, often radiating to the ears, chest, arms or shoulders, local tenderness and swelling, moderate fever, dysphagia and dyspnea. Occasionally, there is also hoarseness. Recovery is the rule, although death from suffocation has occurred. It is not improbable that the disease may sometimes effect changes in the gland leading to hyperthyroidism or to hypothyroidism. The **treatment** is that of the primary condition, with ice locally, and incision in the event of suppuration

## MALIGNANT TUMORS OF THE THYROID

Malignant disease of the thyroid is comparatively infrequent, particularly in this country. Women are more subject to it than men and the majority of cases occur between the ages of 40 and 60. A history of preceding goiter is obtainable in more than half of the cases. Adenocarcinoma and sarcoma are the most frequent types of tumor. Metastasis to the regional lymph-nodes and to distant structures, such as the lungs and the bones, especially those of the skull and face, is extremely common. The metastases in the bones are usually solitary.

Malignant tumors of the thyroid often remain unrecognized for a considerable time, being entirely overlooked or mistaken for simple goiter. Unilateral enlargement of the gland at the cancer age, especially if it develops rapidly and is nodular should arouse suspicion.

Rapid growth of a long quiescent goiter, increasing hardness of the swelling, fixation of the gland to adjacent structures and the overlying skin, local tenderness and pain in the shoulders or behind the ears are also suggestive

[1] Quoted by Curschmann, Nothnagel's Spec. Path. u. Ther.

features. Not rarely, however, metastasis occurs before there is obvious involvement of the thyroid. Unless secondary growths can be demonstrated in the lungs, bones or elsewhere, the treatment should be surgical. Radium and x-ray applications are also useful. Metastases may occur several years after removal of the gland. There was no evidence of recurrence in from 1 to 5 years in 35 per cent. of 65 operative cases of thyroid carcinoma, reported by Balfour[1] of the Mayo clinic.

## DISEASES OF THE ADRENALS

The adrenals are composed of two portions: The cortex, derived from a part of the mesodermal ridge, and the medulla, derived from the sympathetic nervous system. The cortex is especially rich in lipoids, as well as in ordinary fats. The medulla consists in large part of polymorphous cells which stain brown with chrome salts, and hence are spoken of as chromaffin cells. Similar cells are also found along the sympathetic trunks, in the Zuckerhandl body, which is situated near the bifurcation of the aorta, in the intercarotid glands and sometimes in accessory adrenal masses, although the latter are composed, as a rule, only of medullary tissue. A function peculiar to the chromaffin system generally is the production of epinephrin (adrenalin). Complete removal of the adrenals, as Brown-Séquard first showed (1858), is rapidly fatal, although little is known of the manner in which death is brought about.

The cortex of the adrenals is believed to be intimately associated with growth and development, especially of the sexual organs. The adrenal hypernephroma, which is composed of cells of cortical origin, is attended in the young by excessive bodily growth and precocious development of the genitals and the secondary sexual characteristics. Atrophy of the adrenals in childhood is thought by some authorities to be associated with the condition of infantilism and premature senility known as progeria. Studies of the action of epinephrin on animals have led to the belief that the function of this substance is to maintain the tonus of the vasoconstrictor nerves and perhaps of the entire sympathetic system, but the actual amount of epinephrin present at any moment, even in the veins of the adrenals, appears to be entirely too small to exert any pressor effect and moreover no prompt fall of blood pressure is observed when the influence of the adrenals is excluded for a time by ligation. The recent studies of Cannon and others indicate that epinephrin is poured out only in times of excitement and that its chief function is to increase the efficiency of the organism for physical strength. As a consequence of the epinephrin discharge the blood is diverted from the splanchnic and cutaneous vessels, which are constricted, to the heart, the lungs, the central nervous system and the skeletal muscles; the bronchioles are dilated, thus insuring better ventilation of the lungs; the liver yields more sugar to the blood, thus affording an abundance of food for the active structures; the number of erythrocytes per cubic millimeter is increased and the efficiency of the muscles is greatly improved.

Addison's disease and lesions of the adrenals are intimately related, probably in the way of diminished glandular activity, but whether the deficiency is chiefly in the medullary portion, as von Neusser and Wiesel[2]

[1] Medical Record, 1918, xciv, 846.

[2] Die Erkrankungen der Nebennieren, Wien und Leipzig, 1910.

believe or chiefly in the cortical portion, as Biedl and Loewy[1] assume, is still undetermined, although the experimental evidence favors the view that it is the cortex which is indispensable to life. Apart from Addison's disease and neoplasms, the adrenals are not often the seat of disease of clinical interest. *Hemorrhage* sometimes occurs into the substance of the gland in the newborn, but its cause is unknown. It may also occur after injury, in acute infections, in chronic cardiac disease, tabes, etc. The symptoms that have been ascribed to it are pain in the upper abdomen, vomiting, diarrhea, tympanites, convulsions and collapse, followed by coma and death within 48 hours (Arnaud, Rolleston). The adrenals are not rarely involved in both *acute* and *chronic tuberculosis*. Fibrocaseous tuberculosis is the change usually associated with Addison's disease, although this change is often found in the adrenals without any symptoms having been present. *Gummatous infiltration* and *fibroid induration* of the adrenals are occasionally observed in syphilis. *Degenerative processes*, such as cloudy swelling, *fatty change*, and *amyloidosis*, occur in the adrenals as in other organs. *Inflammatory conditions* are sometimes seen in sepsis and other infections. The hypothesis of Josué and other French writers that attributes persistent hyperpiesis and arteriosclerosis to hyperplasia of the adrenals, and especially of the chromaffin tissues, has little evidence to support it. The degenerative changes that occur in the aorta of rabbits after repeated injections of epinephrin differ in several respects from those that are seen in the arteriosclerosis of man, and furthermore an amount of epinephrin in the blood sufficient to maintain abnormally high tension in the arteries would at the same time inhibit intestinal peristalsis and also produce glycosuria.

## ADDISON'S DISEASE

**Definition.**—A comparatively rare disease, probably always fatal, associated with and doubtless dependent upon destructive lesions of the adrenals, and characterized clinically by increased pigmentation of the skin, gastrointestinal irritation, lowered blood pressure, and progressive muscular weakness. Thomas Addison[2] of Guy's Hospital, London, was the first to point out the relation between alterations in the adrenals and the group of symptoms constituting the disease that now bears his name.

**Etiology.**—The disease occurs much more frequently in males than in females and is extremely rare in young children and old persons. Trauma seems to have acted as an auxiliary cause in some cases. An association with Graves' disease is occasionally seen.

During the violent bombardment of Nancy, Richard and Etinne[3] observed a case in which Addison's disease appeared and was followed by symptoms of exophthalmic goiter and two other cases in which Addison's disease became superimposed on preëxisting exophthalmic goiter.

**Morbid Anatomy.**—Changes in the adrenals are present in at least 88 per cent. of the cases (Lewin). By far the most common change is tuberculosis, usually the fibrocaseous form. This was present in 211 of 287 cases collected by Lewin. The process is probably always secondary, although not rarely the adrenals appear to be the only organs affected. In 23 cases collected Alexais and Arnaud[4] there was coexisting tuberculosis of the lumbar

[1] Deutsch. Arch. f. klin. Med., 1913, cx.
[2] London Med. Gaz., 1849.
[3] Bull. de la Soc. méd. des Hôp., 1918, xliii, No. 36.
[4] Rev. de méd., 1891, xi.

vertebræ. Occasionally only one of the glands is tuberculous. In a small proportion of cases other lesions than tubercle are found, such as simple atrophy, fibrosis with atrophy, malignant disease, or hemorrhage. In some instances the adrenals appear to be normal, and, on the other hand, extensive changes may be found in them although no symptoms of Addison's disease have been present. Degenerative or inflammatory changes in the semi-lunar ganglia and sympathetic plexuses have been recorded in a number of instances, usually, however, in association with lesions of the adrenals. Hyperplasia of the abdominal lymph-nodes, enlargement of the spleen and persistence of the thymus may also occur.

**Pathogenesis.**—The exact relation of the lesions to the symptoms still remains obscure. Adrenal inadequacy is apparently an essential factor, but it is not clear whether the cortex or the medulla is chiefly concerned. Von Neusser and Wiesel believe that the disease is due chiefly to failure of the medulla and chromaffin system generally, that the participation of the cortex is only secondary and that of the sympathetic ganglia is unimportant. In some cases of Addison's disease, however, the chromaffin system seems to be normal, and furthermore there are observers who regard the changes in the cortex as the essential factor. Cases of extensive adrenal disease without characteristic symptoms may be explained by the greater rapidity of their course, death ensuing before the symptom-complex has had time to develop or by the vicarious activity of accessory adrenal tissue. Cases of Addison's disease with unilateral lesions have been explained on the assumption that the other organ has been functionally inhibited.

**Symptoms.**—The most important symptom is the gradually developing weakness without commensurate loss of flesh or anemia. In advanced cases the patient may be unable to walk across the room or even to sit up in bed without suffering from dyspnea, palpitation, giddiness and faintness. Attacks of syncope are not uncommon. The heart's action is weak and the blood pressure is usually low, in the later stages sometimes falling to 65 or 60. Next to the progressive asthenia the most constant symptom is discoloration of the skin, the tint varying from a yellowish-brown to a smoky gray, or in rare instances, a pronounced black. The pigmentation, while usually more or less general, is especially marked on those parts of the body which are most exposed to sunlight, which are normally rich in pigment, as the areolæ of the nipples, the axillary folds, the genitals and the groins, and which are habitually rubbed or compressed by the clothing, as the waist, where it is encircled by corset or belt. In some instances it occurs also in the mucous membrane of the mouth, appearing in the form of brownish or bluish-black spots or lines. The scleræ are rarely, if ever, affected. The pigmentation usually follows the asthenia, but in exceptional cases it is the first conspicuous symptom. Occasionally it is entirely absent throughout. Gastrointestinal disturbances, especially impairment of appetite, epigastric discomfort, nausea and vomiting, are rarely absent and at times dominate the clinical picture. In the later stages the vomiting may become uncontrollable. The bowels are sluggish, as a rule, but sometimes there is profuse diarrhea. Toward the end acute abdominal symptoms suggestive of appendicitis or peritonitis occasionally supervene. Mental depression, vertigo, headache, and neuralgic pains in various parts of the body, especially in the loins, are by no means uncommon. Anemia, although usually present, is rarely pronounced, and in many cases there is but little emaciation. Sergent[1] describes a "white line," as evidence of adrenal insufficiency. It is obtained by drawing the finger nail or a blunt instrument firmly across the skin, when

[1] L' Insufficience surrenale, Paris, 1902.

a white line instead of the usual red one slowly appears. The phenomenon doubtless depends upon some vasomotor derangement and is not especially significant.

In Addison's disease the blood-sugar concentration is low and the tolerance for glucose is increased.

The course of the disease is usually chronic, lasting from one to three years. Exceptional cases have been reported which have proved fatal within a few months and others in which the duration was seven years or longer. Alternate exacerbations and remissions in the symptoms are often observed. Death usually takes place gradually as a result of the increasing asthenia, but it may occur suddenly and even unexpectedly from syncope. In other cases the terminal stage is marked by delirium, muscular twitchings and coma.

**Diagnosis.**—A positive diagnosis of Addison's disease is scarcely ever warranted unless the three cardinal symptoms—asthenia, pigmentation, and gastric irritability—are present and evidences of other conditions that might produce them are wanting. Other forms of pigmentation must be excluded. The patchy discoloration of the skin occurring in *pregnancy* and in *diseases of the uterus and adnexa* should be recognized by the history and thorough physical examination of the patient; this is true also of the melasma that is occasionally observed with *abdominal growths* (tubercle, carcinoma and lymphoma). The discoloration of the skin resulting from *chronic malaria* and from *pernicious anemia* should offer no difficulty if the blood is carefully examined. *Chronic jaundice* can not readily be mistaken for the pigmentation of Addison's disease, owing to the involvement of the scleræ, although its after-effects may occasionally arouse suspicion. *Hemochromatosis* (bronze diabetes) is indicated by glycosuria and enlargement of the liver.

*Melanosarcoma* with diffuse pigmentation may usually be distinguished by the detection of a primary growth in the choroid and of metastases in the skin. In *argyria* there is a history of the medicinal use of silver, the discoloration is bluish-gray, and constitutional symptoms are absent. *Arsenical pigmentation* does not involve the mouth and is usually associated with hypertrophic processes in the skin or with polyneuritis, as well as with other characteristic symptoms. The diagnosis of the melanoderma known as *vagabond's disease*, which is produced by dirt, lice and exposure to inclement weather, is generally made clear by the history, the presence of scratch marks, and the effects of bathing, nourishing food, etc. In *pellagra* there is sometimes extensive pigmentation, but in this disease patches of dermatitis are usually present or have been present on the exposed parts, diarrhea is an early symptom, the tongue frequently presents fissures or denuded areas, and pronounced psychic disturbances are of common occurrence. In the rare metabolic disorder described as *ochronosis* the cartilages of the ears and the fibrous tissues about the joints are especially pigmented and the urine blackens on exposure to air. The melanoderma that is sometimes observed in *itching skin diseases, scleroderma, generalized neurofibromatosis* (von Recklinghausen's disease), *Hodgkin's disease, exophthalmic goiter, rheumatoid arthritis*, and *chronically recurring purpura* can readily be differentiated, as a rule, by careful observation of other signs and symptoms.

**Prognosis.**—The disease is probably always fatal. Reported instances of recovery have been so exceptional as to suggest an error in diagnosis.

**Treatment.**—Adrenal preparations have been given with benefit in some cases, but on the whole the results have not been satisfactory. From 10 to 20 grains (0.6–1.3 gm.) of the dried extract of the gland may be given by the mouth three times a day. Epinephrin has also been used subcutaneously, but its value is even more doubtful than that of the extract, as there is little

evidence that suprarenal insufficiency is the result of a loss of epinephrin function.

Apart from organotherapy, the chief indication is to conserve in every way the patient's strength. Rest is necessary and should be more or less complete according to the degree of adynamia. The diet should consist of nutritious, easily digestible food. Tonics, especially strychnin, arsenic and iron, are sometimes useful. To combat vomiting, carbonated water, champagne, cerium oxalate, bismuth subcarbonate and diluted hydrocyanic acid should be tried. Sinapisms over the stomach may be of service. Grawitz found gastric lavage effective in two cases. Strong purgatives are inadmissible as they may excite a persistent diarrhea or cause fatal syncope.

## TUMORS OF THE ADRENALS

Tumors of the adrenals may be primary or secondary. Primary tumors are, as a rule, malignant. Of 298 cases of malignant growth among 5155 necropsies, studied by Symmers,[1] the adrenals were the seat of metastases in 23 instances, or in 8 per cent. Those arising from the cortex are known as *hypernephromas* and are composed of a delicate stroma enclosing large clear cells rich in cholsterin esters and other lipoids. They are often bilateral. So-called renal hypernephromas, which are the most common tumor of the kidney in adults, were believed by Grawitz and his followers to be derived from misplaced adrenal tissue, but more recently it has been claimed (Sudeck, Stoerk, Wilson, and Fraser) that they are derived from the tissue of the kidney itself and are, therefore, renal rather than adrenal tumors. The tumors arising from the medulla of the adrenals have been observed chiefly in young children and are apparently neuroblastomas, the cells composing them being small and arranged in the form of rosettes. Secondary tumors of the adrenals are sarcomas or more frequently carcinomas arising in the stomach, breast, liver or bowel.

The clinical features of primary adrenal growths are variable. Not rarely there is a palpable or even a visible mass in the kidney region with pain and increasing debility. With invasion of the renal pelvis there may be hematuria. In some cases the tumor grows very rapidly and not only infiltrates contiguous structures but also gives rise to widespread metastases, especially in the lungs, liver, bones, and larger veins. Occasionally the metastases produce the first conspicuous symptoms. In other cases the tumor grows slowly and remains localized. Adrenal hypernephromas occurring before the onset of puberty are almost always attended by excessive bodily growth and precocious development of the genitals and of the secondary sexual characteristics. The male characteristics predominate, however, even in females. Symptoms of Addison's disease are usually absent in adrenal tumors even if both glands are almost completely destroyed.

## ACROMEGALY; HYPERPITUITARISM

Acromegaly is a chronic disease manifested by exaggerated growth of the skeletal tissues, hard and soft, especially of the extremities, and apparently due to increased functional activity of the anterior portion of the pituitary

[1] Amer. Jour. Med. Sci., Aug., 1917.

body, the result of tumor or hyperplasia. Symptoms resulting from the pressure of an intracranial tumor, from secondary changes in the posterior lobe of the pituitary body, and from disturbances of other endocrinous glands, with which the hypophysis is closely related, are also present in many cases. Moreover, just as Graves' disease may be followed by myxedema, so in the later stages of acromegaly some of the symptoms of hypophyseal insufficiency may supervene, the glandular hypertrophy giving place to glandular atrophy.

The disease, which was first described by Marie in 1886, is closely allied to *gigantism*, the same lesion producing gigantism if it occurs before ossification of the epiphyseal cartilages, acromegaly if it occurs after the epiphyseal union has taken place, and acromegalo-gigantism (Brissaud) if it occurs in the transition period between adolescence and maturity. According to Sternberg 40 per cent. of all giants are acromegalic.

**Etiology.**—The causes leading to acromegaly are obscure. The disease, which is comparatively rare, is most prone to develop in the third and fourth decades, and affects women more frequently than men. Trauma has been noted in a number of instances.

**Morbid Anatomy.**—Enlargement of the hypophysis, due to simple hyperplasia or adenoma, or, more rarely, to adenocarcinoma, or sarcoma, is present in the large majority of cases. The basic lesion, however, appears to be an increase of the acidophilic cells of the anterior lobe. The rare occurrence of acromegaly without enlargement of the hypophysis may be explained on the basis of involutional changes in the gland and secondary atrophy or the proliferation of small remnants of hypophyseal tissue outside of the sella turcica, as in a case reported by Erdheim.[1] The changes in the sella turcica itself vary from deepening of its fossa with bony thickening to extreme distention with atrophy of its walls. The bones of the body, especially those of the skull, hands and feet, are enlarged and more dense than normal. The cartilages and subcutaneous tissues are thickened. The viscera, also, may be enlarged. Occasionally the heart reaches enormous proportions. Fibrosis of the pancreas is an occasional finding. The walls of the arteries and veins are sometimes thickened and sclerotic. Both hypertrophy and atrophy of the thyroid have been described. The gonads are not rarely undeveloped or atrophic.

**Symptoms.**—Paresthesias or vague pains, commonly ascribed to rheumatism, an arrest of menstruation, and a gradual enlargement of the hands, feet and face, involving both bones and soft parts, are usually the earliest symptoms. In the course of time the appearance becomes characteristic. The head is enlarged from above downward, the cranium being the least affected; the supraorbital arches and cheek-bones are prominent; the nose is broad, long and knobby; the lower lip is thick and often everted; and the chin is massive and much elongated (prognathism). The teeth, from widening of the alveolar processes, are often separated, and the tongue is sometimes so large that it interferes with articulation. All the natural lines of the face are accentuated and under the eyes are swollen sacs.

The hands are especially large with the fingers thick, sausage-shaped, and spongy. The feet are similarly affected. Except in gigantism, the long bones are not much altered. The thorax, however, is broad and deep, and kyphosis in the cervicodorsal region is almost always present.

The hair is coarse, the nails are flat, and the voice, owing to thickening of the laryngeal cartilages, is raucous. Thirst, with increase in the quantity of urine, is often observed, and not rarely there is glycosuria or actual diabetes

[1] Ziegler's Beiträge, 1909, lxiv.

mellitus. Borchardt[1] observed glycosuria in 35.5 per cent. of 176 cases of acromegaly. Loss of sexual power and desire is common. Notwithstanding the bulky frame, there is increasing muscular weakness, with depression and lassitude, and eventually there may be almost complete helplessness. Symptoms of cardiac insufficiency sometimes supervene in advanced cases.

Symptoms of intracranial tumor—violent headache, vertigo, impairment of vision, palsy of one or more of the external ocular muscles, etc.—occur in about 50 per cent. of the cases, and occasionally precede the acromegalic phenomena. In cases of this type alterations in the visual fields, the result of pressure on the optic chiasm, are usually a striking feature, the most common and characteristic defect being bitemporal hemianopsia. The usual condition of the optic nerves is one of partial or complete atrophy. Choked disc is comparatively rare (15 per cent.). Bilateral non-pulsating exophthalmos is sometimes observed.

Certain symptoms of Graves' disease or of myxedema may coexist with those of acromegaly, and not rarely pronounced acromegalics present some of the phenomena of hypopituitarism, such as adiposity, high tolerance for sugar, somnolence, etc. In an analysis of 215 collected cases of acromegaly by Anders,[2] evidences of disturbances of the thyroid function were noted in 33 per cent., signs indicative of hypothyroidism being more common than those of hyperthyroidism.

The course of the disease is usually slow extending over several decades, but acute cases lasting only 2 or 3 years are occasionally observed. Gauthier recognizes two stages, the erethic and the cachectic. Death may be due to coma or syncope or to intercurrent disease.

**Diagnosis.**—The diagnosis is difficult only before the occurrence of the peculiar deformities. In doubtful cases roentgen-ray studies are often useful in revealing enlargement of the pituitary fossa. *Osteitis deformans* (*Paget's disease*) affects especially the bones of the cranium and the long bones of the extremities; it makes the skull broad at the top, and usually causes curvature of the femora and tibia, and it is not accompanied by any hyperplasia of the soft parts.

*Hypertrophic pulmonary osteoarthropathy* affects chiefly the terminal phalanges, causes a knob-like swelling of the finger tips and curvature of the nails, and is associated with chronic suppurative disease within the chest, or less frequently, with chronic valvular disease of the heart. *Myxedema* affects the soft tissues exclusively, makes the face round and puffy, and is accompanied by a dry skin, loss of hair, mental dulness and pronounced depression of the basal metabolism. *Syringomyelia* occasionally produces gigantic growth in a hand or foot—cheiromegaly (Hofmann, Marie, Schlesinger)—but otherwise it does not resemble acromegaly.

**Treatment.**—Thyroid extract persistently used is occasionally of value, especially in relieving headache and improving vision. Extract of the pituitary gland seems to have been of service in some cases, particularly after the occurrence of symptoms suggesting hypopituitarism. An extract of the whole gland may be tried and if this fails an extract of the posterior lobe may be substituted. The dosage must be determined by studying the effects of the drug. Mercurial inunctions have been followed by improvement in two or three instances. If the local symptoms are severe one of two surgical operations—decompression or hypophysectomy—may afford relief. Cushing[3] reports 190 operative cases of pituitary disease, only a few of

[1] Zeit. klin. Med., 1908, lxvi, 332.
[2] Amer. Jour Med. Sci., Feb., 1922.
[3] Jour. Amer. Med. Assoc., June 18, 1921.

which, however, were acromegalies, with a mortality of 9.7 per cent. when the transphenoidal route was selected, and a mortality of 7.5 per cent. when the transfrontal route was selected. In Adson's series of 20 cases there were 6 deaths.[1]

## HYPOPITUITARISM

A condition which, in the light of Cushing's observations on the effect of partial hypophysectomy in young animals, seems to be associated with decreased activity of the pituitary in young persons, has been described by Fröhlich and named by Bartels *dystrophia adiposogenitalis*. It is characterized by infantilism, genital hypoplasia, imperfect acquirement of the secondary sexual characteristics, general adiposity, the presence of pads of fat in the pectoral regions and on the hips, and usually by a high sugar tolerance and mental dulness. Polyuria and polyphagia may also form a part of the syndrome. More rarely the patient shows a peculiar feminine habitus with an arrest of development of the sexual organs, but is oversized rather than undersized or is lean instead of fat. Roentgenograms of the skull often show a small sella turcica. If the hypophyseal lesion develops after adolescence there is an approach to Fröhlich's syndrome, although bony and skeletal growth is usually normal or nearly so. Failure of genital development is well marked and with it there is often a tendency to reversive secondary sex phenomena. In males the skin is smooth and soft, the growth of beard is scanty, the breasts are relatively large, the pubic hair has a straight upper border, as in the female, the buttocks are large and the pelvis is broad. In females the skin is coarse, the genitals are poorly developed, the breasts are small, there is a tendency to hairiness, especially on the upper lip and chin, the pubic hair has a pyramidal configuration, the pelvis is narrow and menstrual disturbances (delayed onset, amenorrhea, sterility, etc.) are usually present. Between typical hypopituitarism and the normal condition there are, of course, many degrees of pituitary deficiency.

Larval forms of hypopituitarism or dyspituitarism, shown chiefly by rapid growth, tardy sexual maturity, pubic hair of invert type, ready fatigability, low blood-pressure, slow pulse, vasomotor ataxia, and vagatonia (hyperchlorhydric syndrome, colicky pains, spastic constipation, etc.), are not rarely observed. Other manifestations may be nocturnal enuresis, periodic headaches, and, as in cases cited by L. Pierce Clark,[2] fainting or epileptoid attacks.

The lesion in most cases of pronounced hypopituitarism is a cyst of the pituitary or a tumor in the vicinity of the gland causing compression. Less frequently hydrocephalus is the cause of the endocrine disturbance and, very rarely, as in Madelung's case, direct trauma is responsible for the symptoms. Both in preadolescent and postadolescent hypopituitarism if a tumor is the anatomical cause of the condition, there may be in addition to derangements of development and metabolism, certain pressure symptoms, such as headache, somnolence, impairment of vision, etc. Bitemporal hemianopsia is specially significant.

While both experimental and clinical studies strongly support the view that decreased activity of the pituitary is an important factor in Fröhlich's syndrome and allied conditions, it is not improbable that other endocrinous

[1] Keen's Surgery, 1921, vol. viii, p. 68.
[2] Amer. Jour. Med. Sci., Feb., 1922.

glands are concerned in the process, as the combination of adiposity and sexual infantilism has been observed also in disease of the thyroid, thymus, the sex glands, the pineal body, and even the pancreas (Bramwell, Rentoul).

Two other conditions that seem to be related in some way to changes in the hypophysis and, perhaps, other ductless glands, and which are more nearly the antithesis of acromegaly than Fröhlich's syndrome, are *ateliosis*[1] and *progeria*.[2] The chief features of ateleiosis are a childish facial appearance, diminutive stature, short slender extremities, ill developed muscular prominences, and small jaw bones, with a thin piping voice, low arterial tension and scanty urination. In progeria the body is arrested in its growth and becomes prematurely the subject of senile changes the patient passing directly from delayed childhood to premature old age.

**Treatment.**—In all forms of hypopituitarism both pituitary extract and thyroid extract are worthy of trial. In a number of instances good results have been obtained from one or the other of these remedies. If there is severe headache or failing vision surgical measures (decompression or removal of the growth) should be considered.

## DISEASES OF THE THYMUS

The function of the thymus is not definitely known. Some writers believe that the organ is a lymphoid structure with the function of lymphoid tissue in general, and others regard it as a ductless gland with a function related in some way to that of the sex glands, the hypophysis and the chromaffin tissue. The thymus normally attains its greatest development at the end of the second or third year of life, when it usually weighs from 6 to 10 grams. Atrophy of the gland occurs very gradually from about the third year until puberty, and more rapidly thereafter, so that by the twenty-fifth year, as a rule, only small remnants of the original structure remain. However, it is not uncommon to find in young adults who have died suddenly thymus glands weighing from 5 to 15 grams. Experimental removal of the thymus in young animals has yielded contradictory results, although a considerable number of observers have reported retardation of growth with rachitic-like deformities, especially in the long bones of the legs, and a few have cited certain changes in the endocrine glands. Parke and McClure[3] conclude from the results of their own experiments and from an exhaustive review of the literature that the thymus is not essential to life in the frog, rat or dog, and that thymectomy probably produces no alteration in the organs of internal secretion, but the possibility that it may cause retardation in development and delayed closure of the epiphysis cannot be excluded absolutely.

Pathologic atrophy of the thymus has been observed in cases of fatal marasmus in children, but probably as the effect of the general malnutrition rather than its cause. Enlargement of the thymus occurs in a number of diverse conditions, such as exopthalmic goiter, acromegaly, Addison's disease, myasthenia gravis, rachitis, Hodgkin's disease and leukemia, as well as in neoplasms (lymphosarcoma, carcinoma, dermoid cyst) involving the gland itself. Occasionally, the thymus is affected secondarily, also, in the course of such infectious processes as septicopyemia, syphilis, and tubercu-

[1] Gilford: Trans. Med.-Chir. Soc., 1902.
[2] Gilford: "The Disorders of Post-natal Growth and Development," 1911.
[3] Amer. Jour. Dis. Children, Nov., 1919.

losis. From a clinical viewpoint, however, the most important enlargement of the organ is that which is found in association with so-called thymic asthma or thymic death and the status lymphaticus.

## THYMIC ASTHMA; STATUS LYMPHATICUS

**(Persistence of the thymus; Thymic Death; Lymphatism)**

The term thymic asthma has been applied to a comparatively rare condition, observed usually in children but occasionally, also, in adults, which is characterized by thymic enlargement, paroxysms of dyspnea, and a pronounced predisposition to sudden death.

The enlargement of the thymus is a hyperplasia of unknown cause. The gland may weigh from 15 to 50 grams or more. Occasionally, as in cases cited by Hedinger[1] several members of one family are affected. The respiratory difficulty, which appears, as a rule, soon after birth, varies in degree from a slight stridor, chiefly inspiratory, to severe suffocative attacks of an asthmatic character. The attacks may occur without apparent cause or may be precipitated by crying, coughing or throwing the head backward. Between them the respiration may be entirely normal or there may be more or less stridulous dyspnea. Recovery may gradually ensue after the second or third year, but more frequently the symptoms increase in severity until finally a paroxysm proves fatal. In other cases sudden death occurs from trivial or unapparent causes without there having been any antecedent stridor or dyspnea, the child becoming cyanotic, losing consciousness and dying within a few minutes (*thymic death*). Such fatalities have occurred in seemingly healthy children during the ordinary course of their daily life, or in relation to some such occurrence as fright, a cold bath, the administration of an anesthetic, especially chloroform, a subcutaneous injection, or even the use of a tongue depressor. In a third group of cases thymic asthma or thymic death is the chief feature of the condition known as the *status lymphaticus* (Paltauf[2]). In this condition there is hyperplasia not only of the thymus but also of the lymphatic tissues throughout the body. The patients are usually pale, flabby and somewhat fat. The tonsils and adenoid tissues of the throat are hyperplastic, sometimes to an extreme degree. The spleen is often palpable and the superficial lymph-nodes are not rarely enlarged. There is usually some degree of anemia with lymphocytosis. The general resistance is weak. Attacks of syncope are not uncommon. Evidences of rickets are frequently present and in many cases other morbid conditions also occur in association, the commonest being infantile eclampsia, tetany, epilepsy, and infantilism with imperfect development of the secondary sex characteristics. Some doubt exists as to whether the status lymphaticus is a definite morbid entity.

Inspection and palpation are negative in thymic hyperplasia, except in the rare cases in which the gland is very large and forms a visible and palpable swelling in the suprasternal notch. Percussion occasionally reveals abnormal dulness on both sides of the manubrium and auscultation may disclose abnormal tracheal sounds. The voice is unchanged. Radiography is a valuable diagnostic aid. In a case reported by Chevalier Jackson the condition was recognized by tracheoscopic examination after tracheotomy. As to the cause of death there is a great difference of opinion. Mechanical pres-

[1] Deutsch. Arch. f. klin. Med., 1905, lxxxvi.
[2] Wien. klin. Woch., 1889, No. 46; 1890, No. 9.

sure on the trachea is undoubtedly a factor in a small proportion of cases. Pressure on the large vessels, on the nerves (vagus, sympathetic), and on the heart itself have each in turn been suggested as the cause of the suffocation or cardiac paralysis.

Caution is necessary in making the **diagnosis** of thymic enlargement, as stridulous dyspnea in infants has several causes, such as enlargement of the tracheal or bronchial lymph-nodes, retropharyngeal abscess, membranous laryngitis, ordinary laryngismus, and congenital malformation of the laryngeal vestibule.

**Treatment.**—General hygienic measures that will tend to improve the patient's nutrition and increase the resistance to infection are indicated. Rickets, if present, should be carefully treated. Emotional excitement, excessive physical exertion, cold bathing, surgical operations, and all other provocatives of attacks should be avoided. During attacks the child should be kept in a horizontal position, warm applications should be made to the neck, and cardiac stimulants should be given, if necessary. Unless relief is afforded intubation with a long tube should be practised. The x-ray may be of service in reducing the size of thymus. In a number of cases thymic enlargement with pressure symptoms, operation (complete or partial thymectomy, decompression by resection of the manubrium, elevating and suturing) has given good results. According to DaCosta[1] in 42 reported cases of thymectomy there were 15 deaths.

[1] Da Costa: Modern Surgery, 1919, Eighth edition, p. 1390.

# Diseases of the Joints and Bones

## ARTHRITIS DEFORMANS

(Chronic Osteo-arthritis; Rheumatoid Arthritis)

**Definition.**—The term arthritis deformans is here used to designate a common form of chronic non-suppurative arthritis, which is commonly polyarticular, which has a marked tendency to cause permanent stiffness and deformity of the affected joints, which is usually, if not invariably, of infectious origin, and which is clearly not the result of trauma, gout, rheumatism, acute gonorrhea, infectious granulomatous processes (tuberculosis, syphilis), organic nervous disease (tabes, syringomyelia) or hemorrhagic conditions (hemophilia, purpura, etc.).

The disease is of great antiquity. The deformities produced by it have been found in Egyptian mummies at least 5000 years old. Very little was known about it, however, until the nineteenth century. In 1800 Landré-Beauvais recognized arthritis deformans as a modification of gout and a few years later Heberden and Haygarth each clearly distinguished it from both gout and rheumatism. In 1836 Adams, of Dublin, gave a full and accurate account of it.

**Pathology.**—No satisfactory classification of the cases of arthritis deformans is at present possible, but the one that has been suggested by Nichols and Richardson,[1] and which is based on the pathological changes occurring in the joints, seems to square best with the clinical manifestations of the disease. These investigators, whose deductions are drawn from a pathological and clinical study of 65 cases of arthritis deformans, recognize two distinct types of the disease: (1) A *proliferative type* which tends to destroy the articular cartilage and lead to ankylosis of adjacent articular surfaces, and (2) a *degenerative type*, which tends to destroy the articular cartilages and produce a deformity without ankylosis. Nichols and Richardson believe that these types do not correspond to two distinct diseases and that they may even coexist in the same patient, and thus are in accord with Nathan,[2] who maintains that the variations in the morbid process are determined not by the specificity of the inciting agent but by its virulence, the resistance of the host, and its exact localization in the joint.

*Proliferative Arthritis* (*Atrophic Arthritis, Chronic Progressive Polyarthritis*).—Granulation tissue appears upon the synovial membrane and sometimes also in the connective tissue of the epiphyseal marrow and by extension from one or the other of these localities leads to destruction of cartilage, which eventually may be complete. At the same time there is proliferation of the perichondrium, resulting in the formation of new cartilage or bone and also proliferation of the endosteum of the epiphysis, resulting in the formation of trabeculæ of osteoid tissue. With the destruction of the intervening cartilage, fusion of the opposing layers of new tissue occurs, causing partial or complete ankylosis and obliteration of the joint cavity. If the synovial granulation tissue predominates, ankylosis is fibrous; if perichondrial proliferation predominates, it is cartilaginous; if trabecular pro-

[1] Jour. of Med. Research, N. S., 1909, xvi.
[2] Jour. of Med. Research, 1917, xxxvi.

liferation predominates, it is bony (Nichols and Richardson). There is little tendency to eburnation, and bony formation at the periphery of the joint is rare, restricted motion being due to ankylosis rather than to the presence of osteophytes. Detached particles of synovial tissue ("joint mice") within the joint are not often observed. The capsule of the joint is always more or less thickened throughout. Partial luxations are common.

*Degenerative Arthritis* (*Hypertrophic Arthritis*).—In this type the primary change consists in fibrillation, degeneration and erosion of the articular cartilage, with exposure of one or both bone-ends, compensatory hyperplasia of the remaining cartilage, and marked irregularity of the articular surfaces. Coincident with the destruction of cartilage the trabeculæ of the epiphysis become thickened and a new formation of osteoid tissue occurs and is later converted into bone, the final result being obliteration of the marrow spaces and great condensation of the bone-ends, which are often highly polished or eburnated as a result of friction.

Another important change in this type of arthritis is an irregular, nodular hyperplasia of the perichondrium at the junction of the cartilage and capsule, with the transformation of the new tissue into cartilage and then into bone, the latter sometimes becoming eroded and eburnated like the original bone-ends. Small polypoid masses of fibrous tissue, cartilage or bone frequently project into the joint or become detached, constituting so-called "joint mice." Thickening of the capsule is, as a rule, not marked, changes in the synovial membrane occur only after there has been extensive destruction of cartilage, and true ankylosis with complete obliteration of the joint cavity is not observed. The compensatory hyperplasia of the articular cartilage and the peripheral perichondrial new formation of cartilage and bone (osteophytes) usually cause marked enlargement and deformity of the joint, but do not often completely destroy functional power. However, serious interference with motion may occur if the deposit of osteophytes becomes excessive or interlocking of the bones or subluxation ensues in consequence of the great unevenness of the articular surfaces.

**Etiology.**—Arthritis deformans may occur at any *age*. The proliferative or atrophic type is observed most commonly in young adults, although it is not rare in children. The form described by Still occurs almost exclusively in the young. Degenerative or hypertrophic arthritis is seen chiefly in middle life and old age, and is infrequent in childhood. *Enfeeblement of health* from unfavorable hygienic surroundings, poor food, overwork, prolonged mental strain, etc. is usually regarded as a predisposing factor. In women prolonged lactation and frequent childbearing are also believed to favor the occurrence of deforming arthritis.

*Mechanical injury*, whether it be a sudden severe traumatism or continuous strain incidental to occupation is not without influence, and often serves to intensify the process in certain joints or even to localize it. Preiser maintains that *disturbances in the static relations of the joint surfaces*, such as may occur in the hip as a result of slight deviations in the pelvic obliquity, sometimes play an important etiologic rôle.

The essential cause of the disease is not always apparent, but the evidence in favor of the view that *infection* is the predominant factor in the majority of cases, if not in all, is very strong. Occasionally, arthritis deformans follows one of the general infections, such as puerperal septicemia, pneumonia, influenza and meningitis, but much more frequently it is secondary to chronic focal infection in the tonsils, accessory sinuses of the nose, teeth, gums, genito-urinary tract, middle ear, gall-bladder, appendix, or renal pelvis. In some instances the infection appears to have its source in the colon. In

children the chief portal of infection is in the tonsils and adenoids. Not rarely no infective focus can be demonstrated. Various organisms seem to be capable of inciting the disease, but streptococci, especially *S. non-hæmolyticus* (*viridans*) and *S. hæmolyticus*, have been met with most frequently. Bacteriologic examination of the articular exudate and of the blood is often negative and for this reason it has been suggested that bacterial toxins rather than bacteria themselves may be a factor in producing the disease or in perpetuating it once it has been established. However, Rosenow[1] and others have repeatedly found organisms in the lymph-nodes draining the affected joints when exudate from the latter was apparently sterile.

Whether *disturbances of metabolism* can of themselves excite arthritis deformans is somewhat doubtful, although agents that have an important influence on metabolic activity, such as thyroid extract, arsenic, and the x-ray, not rarely do good in the disease, and Pemberton[2] and others have found that a reduction in the intake of carbohydrate and protein food, either by modifying bacterial activity in the bowel or in some other way, proves beneficial in many cases. Possibly, a metabolic disturbance may be able to maintain changes in the joints, once these have been produced, even though it is without power to initiate them.

**Symptoms of Proliferative Arthritis or Chronic Progressive Polyarthritis.** In many cases the onset is more or less sudden, with a moderate rise of temperature (100°–103° F.), a pronounced increase in the pulse-rate and other constitutional disturbances. A number of joints, simultaneously or consecutively, become painful, swollen, and sometimes slightly reddened. Those of the hands and feet are especially likely to suffer. Of the large joints, the knees and elbows are much more frequently attacked than the hips and shoulders. The thumbs and great toes usually escape. Certain joints, such as the temporomaxillary, sternoclavicular, and those of the cervical vertebræ, which are usually spared in rheumatism, are often involved in arthritis deformans. A joint that is once affected does not usually become free again until the attack is over. In the majority of cases the lesions are definitely symmetrical. Muscular atrophy commonly appears early and is especially marked in the hands, where with the peculiar fusiform or spindle-shaped swellings of the interphalangeal joints, it forms a very typical picture. The persistence of a high pulse-rate (90–110) for weeks or even months after the temperature has returned to normal is a significant feature in many instances. Sweating of the entire body is not so often observed as in rheumatism, but the hands and feet are usually clammy. Not rarely the lymph-nodes in association with the affected joints are slightly swollen. Pallor is often noticeable early in the disease; yet, as a rule, there is little actual anemia. The leucocyte count may be normal, but a moderate increase is sometimes observed.

The disease may pursue one of three courses. First, it may continue for a period of from two to six or eight weeks and then completely subside leaving the joints in a normal condition. Occasionally there is no recurrence, but as a rule, other attacks follow at intervals of from a few months to several years, and at length the joints become permanently crippled. Secondly, in many cases the attack does not end in perfect recovery, but leaves behind slight swelling and stiffness of the joints, which slowly increase, sometimes steadily, but at other times with longer or shorter remissions, until after a

[1] Jour. Amer. Med. Assoc., April 11, 1914.

[2] Amer. Jour. Med. Sci., 1912, cxliv, 744; *Ibid.*, 1913, cxlv, 423; *Ibid.*, 1916, cli, 351; Jour. Amer. Med. Assoc., 1920, xxvi, 1759.

time, perhaps years, there is complete disability. Thirdly, the affected joints, or a certain number of them, may become stiff and deformed early in the case and may remain so permanently. Thus, in a single attack and in the course of a few weeks the patient may be made more or less of a cripple for life.

In some cases of proliferative arthritis deformans the symptoms develop insidiously and advance slowly, joint after joint becoming stiff and deformed. The course of the disease may be uniformly progressive, but usually it is marked by recurring exacerbations, each of which is accompanied by slight pyrexia and is followed by increased maiming. While the disease often reaches an inactive stage before many joints have been destroyed, it sometimes continues to spread until nearly every articulation in the body is affected and the patient becomes absolutely helpless and as rigid as a wooden image. Pain varies greatly, often it is well borne, but it may be severe, especially during the exacerbations. In cases beginning insidiously the articular changes are frequently foreshadowed by neuralgic pains or other sensory disturbances, such as numbness, formication, and a sense of fatigue. Muscular atrophy is almost always a conspicuous feature. It is especially noticeable in the hands and forearms, but in severe cases it may be nearly universal. In time the affected muscles undergo contraction and thus the disability and deformity that have already been produced by destruction of the articular cartilages are considerably increased. Various distortions are observed. The larger joints are, as a rule, in the position of flexion. In many instances the hands are characteristically affected, the fingers deviating to the ulnar side and the proximal knuckles of the forefingers projecting toward the thumb. When the articular surfaces are moved upon one another a peculiar creaking or grating sensation is often observed. Subluxations and ankylosis of varying degrees and of different varieties not rarely occur. In addition to the muscular atrophy there are other indications of disturbed nutrition. The skin over the affected joints is often smooth and glossy; sometimes it is livid and mottled. Areas of brown pigmentation occasionally appear about the forearms, under the eyes, or across the forehead. In many cases the nails are rough and brittle.

In advanced cases of proliferative arthritis the x-ray shows atrophy of the bones in the neighborhood of the affected joints with increased permeability and, in many cases, a disappearance of the joint-slits.

**Degenerative Arthritis (Hypertrophic Arthritis).**—This form occurs, as a rule, at a later period of life than proliferative arthritis. A history of traumatism is common. The lesions may be confined to a single joint or may affect several joints. General polyarticular involvement, however, is rarely observed. The hips, the shoulders and the knees are the joints most often affected. A common example is the arthritis occurring in the hips of old persons (morbus coxæ senilis). The onset is gradual, and frequently for months or even years pain and stiffness on movement are the only symptoms. In some instances the pain is of a neuralgic character and follows the course of nerves that are in relation with the affected joints. Thus, sciatica is often the expression of an arthritis affecting the lumbo-sacral or sacro-iliac joints. After a time the diseased joint shows some enlargement, but this, unlike the fusiform swelling of the proliferative type, is irregular and nodular. Owing to the slow destruction of the cartilages, true ankylosis does not occur, although eventually motion may be considerably restricted as a result of interlocking of exostoses or of the bones themselves, luxation, or the lodgment of synovial tags between the articular surfaces. Recurrent attacks of acute synovitis characterized by effusion into the joint, tenderness and

increased pain, due to traumatism, interlocking of bones or pinching of synovial outgrowths, frequently mark the course of the disease. X-ray examinaton shows perichondrial nodosities, enlargement and increased density of the bone ends, irregularity of the articular surface and usually a well defined joint space. The general health of the patient is, as a rule, but little affected.

**Deforming Arthritides of the Spine.**—Both varieties of deforming arthritis occur in the spine. In the proliferative variety (*spondylitis chronica ankylopoietica*) there is a marked tendency to intracapsular ankylosis; in the degenerative variety (*spondylitis deformans*) the conspicuous features are the presence of exostoses on the bodies of the vertebra and "lipping" of the latter at the edge of the intervertebral discs. Other joints, especially the hips and shoulders, are frequently involved coincidently with the spine or at a later period (*spondylose rhizomélique of Marie*). The chief symptoms of the disease are pain in the back radiating to the trunk or the extremities, limitation of the movements of the spine, with the gradual development of rigidity, and alteration in the natural curves of the spine. The pain varies much in severity and often decreases as the disease advances. It is always worse after rest. In some instances involvement of the nerve-roots gives rise to referred pain closely simulating that of tabetic crises, gall-stones, renal calculus, or prostatic disease. Sciatica and lumbago frequently have their origin in spondylitis. Restriction of movement is made evident by rotation of the head, bending the body or stooping. Both the pain and the stiffness are usually worse on one side than on the other. With involvement of the costo-vertebral articulations there may be pain on breathing or even complete absence of thoracic respiration. The most common deformities are pronounced exaggeration of the dorsal curve (kyphosis), loss of the lumbar curve and flattening of the chest. Both the existence of the disease and its type are usually well shown by the x-ray.

**Still's Disease.**—This peculiar form of arthritis deformans, named after G. F. Still,[1] who first described it, occurs almost exclusively in children. It is a polyarthritis with an acute or a gradual onset, involving the soft tissues of the joints. Its distinctive features are enlargement of the lymph-nodes, especially those draining the affected joints, and enlargement of the spleen. Marked cachexia frequently develops and not rarely the disease results in arrested growth. There is no tendency to actual ankylosis or to the formation of osteophytes, but more or less disability is likely to ensue.

**Heberden's Nodes.**—These are small bony or cartilaginous knobs, about the size of a pea, occurring at the base of the terminal phalanges of the fingers in persons, particularly women, who have reached the middle period of life. They are usually regarded as representing the mildest form of arthritis deformans, although similar excrescences occasionally occur also in gout. In many cases no other evidences of arthritis appear. The nodes usually persist through life, but rarely cause pain or serious hindrance to the free use of the fingers.

**Complications of Arthritis Deformans.**—*Endocarditis*, *pericarditis* and *pleurisy* sometimes occur, more particularly during acute phases of the disease, but are much less common than in true rheumatic polyarthritis. Varying degrees of *myositis* often accompany deforming arthritis, and not rarely *neuritis* ensues as a result of the extension of the inflammatory process or of compression of the nerves by bony or cartilaginous proliferations.

**Diagnosis.**—The points distinguishing arthritis deformans from *rheumatism* and from *gout* are considered on pages 253 and 359 respectively. Arth-

[1] Trans. Royal Med.-Chirurg. Soc., lxxx, 1897.

ritides that are definitely the result of specific infections, such a *gonorrhea, typhoid fever, tuberculosis*, etc., are not usually difficult to exclude. Other arthropathies from which arthritis deformans must be distinguished are the following:

*Charcot's Joints.*—The arthropathies that occur in from 4 to 6 per cent. of all tabetics and in from 20 to 25 per cent. of all syringomyelics are usually unmistakable. It is only the very early cases that resemble arthritis deformans and even in these an error in diagnosis will almost never occur if the possibility of a spinal cord disease is borne in mind. Important features are the sudden onset, absence of pain and fever, enormous distention and rapid disorganization of the joint, and the usual flail-like motion that ensues.

*Secondary Hypertrophic Osteoarthropathy.*—This chronic condition, first described by von Bamberger[1] and later named *hypertrophic pulmonary osteoarthropathy* by Marie,[2] appears to be closely related to arthritis deformans. It is manifested by painful enlargement of the hands and feet and of the distal ends of certain long bones, chiefly those of the forearms and legs, and usually by marked clubbing ("parrot-beaked incurvation") of the fingers and toes. The lesions are symmetrical. Nearly 50 per cent. of the recorded cases (144 in 1915[3]) occurred in association with disease of the respiratory tract, especially tuberculosis, bronchiectasis, empyema, or malignant tumor. Most of the remaining cases occurred in the course of congenital heart disease, hypertrophic cirrhosis of the liver, or chronic diarrhea. Briefly stated, the lesions consist in osseous deposits beneath the periosteum of the long bones, serous effusion into the joints, erosion of the articular cartilages and thickening of the periarticular tissues. The immediate cause of these changes is somewhat obscure. Von Bamberger, Marie, and Sternberg believe that they are toxigenic. Prolonged venous stasis appears to be an important factor in some cases and an accessory one in others. Ordinary clubbing of the fingers, which occurs so frequently in pulmonary tuberculosis, is usually conceded to represent the first stage of hypertrophic pulmonary osteoarthropathy.

*Hemophilic Arthritis.*—This condition is usually observed in early life and attacks the knee in nearly half of the cases, the elbow in about one-fourth of the cases, and the ankle next in frequency. The joint becomes infiltrated with blood, usually spontaneously, but sometimes in consequence of a trivial injury. The swelling is rapidly followed by signs of a mild synovitis. Ecchymoses frequently appear around the joint within a few days. The attack subsides in a short time, but recurrence is the rule, and eventually a form of chronic arthritis may be produced resembling arthritis deformans. Careful attention to the patient's history and to the succession of symptoms, however, will usually prevent any error in diagnosis.

*Syphilitic Arthropathies.*—Lesions of the joints are relatively frequent in hereditary lues, but somewhat uncommon in the acquired form of the disease. The resemblance to arthritis deformans may be very close, but the condition is, as a rule, monarticular and almost always accompanied by a proliferative periostitis. Other symptoms of syphilis, a positive Wassermann reaction and a favorable response to antiluetic treatment are aids to diagnosis.

*Deforming Osteochondritis in Children.*—This rare disease, to which Legg[4] in 1910 and Perthes[5] in 1913 first drew attention, occurs in children,

[1] Wien. klin. Woch., 1889, ii, S. 225.
[2] Revue de Med., 1890, x, I.
[3] Locke, Arch. Int. Med., May, 1915.
[4] Boston Med. and Surg. Jour., Feb. 17, 1910.
[5] Archiv. f. klin. Chirurg., 1913, ci, No. 3.

usually boys, between the ages of 5 and 10 and affects one of the hip-joints. Limping, absence of pain and of reflex rigidity of the muscles, and resistance to rotation, and especially to abduction, without limitation of flexion are the chief features. The x-ray shows a destructive process in the interior of the head of the femur and atrophy of the epiphysis, but no indications of arthritis. The condition is comparatively harmless, always yielding satisfactorily to appropriate treatment and often subsiding spontaneously.

*Intermittent Hydrarthrosis.*—This rare condition, first described by Perrin in 1845, appears to be closely related to angioneurotic edema, and therefore is probably a vasomotor neurosis, although the possibility of its being an anaphylactic manifestation, at least in some cases, must be admitted. The symptoms are characteristic: Suddenly, and often without warning, one joint, usually the knee, or several joints become swollen. The swelling continues for a few days, rarely longer, and then rapidly disappears leaving the joint perfectly normal. Pain, if present, is not often severe. The attacks are repeated during months or years at intervals varying in length in different cases, but in many instances fairly regular for each individual. In many of the 57 cases analyzed by Benda[1] other nervous disorders, including asthma, nervous diarrhea, epilepsy and the circumscribed edema of Quincke, were also present. The periodicity of the attacks, the absence of inflammatory features, and the rapid return of the joint to its normal condition distinguish the disease from acute arthritis deformans.

*Hysterical affections of the joints* are exceedingly rare, at least in America, and, as a rule, involve only one articulation, most frequently the hip or the knee. Charcot states that of 70 cases 38 involved the knee and 18 the hip. The condition may be differentiated from arthritis deformans by the absence of inflammatory features, the association of other hysteric symptoms, and the fact that the pain is usually greater upon light friction than upon deep pressure. Roentgenography and examination under anesthesia will aid materially in the diagnosis.

Arthritis deformans of the spine must be distinguished from Pott's disease, syphilitic spondylitis, typhoid spine, traumatic spondylitis, malignant disease of the spine, chronic cervical pachymeningitis, and perinephric abscess. In doubtful cases the anamnesis, the data obtained from a complete physical examination, and the roentgenographic findings will usually clear up the diagnosis.

**Prognosis.**—The outlook is uncertain. In some cases the disease becomes inactive before there is any actual disabling and remains so indefinitely or even permanently. In other cases, despite all treatment, it progresses steadily or by relapses until many of the joints become distorted and functionless. One is often misled into regarding a prolonged remission as a complete cure. Generally speaking, the most favorable cases are those in which there is a definite focus of infection, especially in the tonsils or teeth, and in which the joints have not yet become seriously damaged. However, removal of what appears to be the primary source of infection does not always produce the desired effect. Failure is common, and may be due to the existence of a less conspicuous but more important focus of infection elsewhere in the body, to the power of the process in the joints, once it has been established, to perpetuate itself, even after the primary cause has ceased to act, or to the operation of some factor other than infection. Of course, no treatment can restore function in the joints after the articular cartilages have been destroyed.

**Treatment.**—The chief indications are to get rid of the original focus or

[1] Allg. Med. Central-Zeit., 1900.

foci of infection, to increase the patient's powers of resistance, to relieve pain, and to secure the maximum amount of efficiency in the affected joints. In searching for primary sources of infection it is often necessary to enlist the services of a skilled dentist, roentgenologist, rhinologist or genito-urinary surgeon. So far as the teeth are concerned, it must be borne in mind that alveolar abscesses may be present without producing pain or any changes in the mouth that are evident on ordinary inspection. X-ray examination is usually necessary, but interpretation of the findings requires much experience and good judgment. Removal of teeth is justifiable only when there are definite indications of deep-seated infection.

The diet should consist of easily assimilable food and, as a rule, should be liberal. In some cases, however, especially when no infective foci can be found or when infective foci have been removed without benefit to the patient a reduction of the intake of carbohydrate and protein food below the level of that to which the patient has been accustomed may yield very satisfactory results. For the details of this treatment by reduced diet, the reader should consult the papers of Pemberton,[1] to which reference has already been made. If the patient is well nourished or obese the intake of food may sometimes be reduced as much as 1000 calories with advantage. To guard against too great a loss of weight, the carbohydrates and proteins that have been withdrawn from the diet may be replaced in part by fats—butter, cream, olive oil, codliver oil. Of course, severe dietetic restrictions are out of place if the patient is already anemic and emaciated.

General hygienic measures are of great importance. The patient must be warmly clothed, must have his bowels moved at least once daily, must keep his skin active by frequent bathing, must take water freely, and must be protected from wet and sudden changes of temperature. A change of climate, especially in cases that are not far advanced, frequently exerts a favorable influence. Visits to hot mineral springs (Hot Springs of Virginia or Arkansas, Bath, Baden-Baden) are often helpful. Residence in a dry, warm climate—Southern California, Arizona, Riviera, Egypt—particularly during the changeable seasons, may in itself be productive of much good.

A cheerful environment, with an abundance of sunshine and fresh air, and hydrotherapy, particularly in the form of an alternating hot and cold douche or spray applied to the spine with considerable force for a few minutes every other day or every day, are valuable adjuvants to other therapeutic measures. Absolute rest is necessary in every case as long as motion causes pain.

The most generally useful drugs are the syrup of ferrous iodid and arsenous acid. The former may be given in doses of 20–30 minims (1.2–2.0 mils) and the latter in doses of $\frac{1}{60}$–$\frac{1}{40}$ grain (0.001–0.0016 gm.), three times a day after meals. Endocrine therapy is beneficial in some cases. Thymus extract (5–10 grains—0.3–0.6 gm.), pituitary extract (5 grains–0.3 gm. of the whole gland), or thyroid extract (1–2 grains—0.06–0.13 gm.) three times a day may be tried, but the effects of the last must be carefully observed.

Vaccines, especially if autogenous, are of real value during the more acute stages of the disease in a small proportion of cases, but they must never be used as a substitute for the removal of the causative infection, if this can be located and its eradication is feasible. The dose is 10 million killed microorganisms, increased, if necessary, to 2 billion, every 4 to 7 days. The intravenous injection of a non-specific protein antigen, although sometimes productive of severe reactions, is on the whole as effective as specific bacterial

[1] *Loc. cit.*

vaccination. Killed typhoid bacilli may be used for the purpose, the dose being 75 million to 200 million every two or three days, or in rare instances as often as once a day. Salicylates and phenylcinchoninic acid (atophan) are useful as analgesics, but have no influence on the disease itself. General tonics, especially iron and nux vomica, are frequently required in anemic and emaciated patients. Codliver oil, in such doses as the stomach will tolerate, may also be of service, if there is much malnutrition.

*Local Treatment.*—Rest of the affected joints until motion no longer causes pain is essential. If necessary, bandages or splints should be employed to insure the immobilization. Tincture of iodin, liniments containing methyl salicylate, an ice-bag, or a hot water bag may be employed to relieve pain. High frequency and static electricity also have an anodyne effect. Local hyperemia produced by Bier's constriction method is useful in some cases. Bandaging the limbs often serves to overcome the muscle-spasm that occurs especially at night and interferes with sleep. After all the acute symptoms have subsided light massage and passive exercise should be begun, the amount of each being determined by its effect on the patient. As the case progresses active exercise should be added and gradually increased. Local stimulation by alternating douches of hot and cold water is also of value. Baking sometimes gives excellent results, but it should never be employed in the acute stage of the disease. Goldthwaite, Painter and Osgood[1] speak favorably of applications of the high-frequency current over the affected joints. Various operative procedures, such as forced disruption of adhesions, arthrotomy, arthrodesis and arthroplasty, are sometimes indicated in advanced cases.

## OXYCEPHALUS

The term oxycephalus is applied to a rare condition, dating from birth or occurring in the first few years of life, characterized by a peculiar deformity of the cranium, impairment of vision, and exophthalmos, usually with external strabismus and nystagmus. The cranial deformity consists of enlargement of the entire anterior portion of the vault "(thurmschädel" type), and

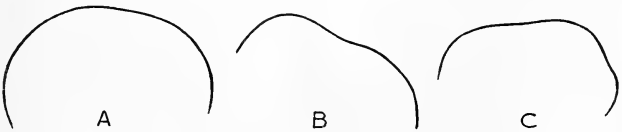


FIG. 31.—Lateral outlines of skulls in (A) hydrocephalus; (B) oxycephalus; (C) rickets.

in the more severe cases bulging of the anterior fontanelle. The amaurosis is the result of secondary optic atrophy, and the exophthalmos, of the shallow orbits. Severe headaches and epileptiform attacks frequently develop in the more severe cases, and not rarely other malformations, such as asymmetry of the face, contraction of the nares with adenoid growths, a highly vaulted palate, webbed fingers, etc., are present in addition to the oxycephalic skull. The intelligence is unimpaired. Premature synostosis of the bones forming the posterior portion of the skull, with resulting increase in the intracranial pressure and growth of the brain only in the anterior direc-

[1] Diseases of the Bones and Joints, 1909, p. 317.

tion, has been suggested as the cause of the syndrome. There are, as a rule, no evidences of rickets, and at autopsy neither hydrocephalus nor signs of meningitis are found. Patients with pronounced pressure symptoms usually succumb before puberty. In several cases reported by Sharpe[1] the operation of cranial decompression yielded good results.

## OSTEITIS DEFORMANS

### (Paget's Disease)

Osteitis deformans is a comparatively rare disease characterized by gradual thickening and deformity of the bones, especially the calvarium, spine, and larger long bones of the extremities. It was first described by Paget[2] in 1876, although Czerny had previously applied the term to another affection.

**Etiology.**—The cause of the disease is unknown. Heredity is a factor in some instances. Males are affected about twice as frequently as females. The condition usually comes under observation in middle life.

**Morbid Anatomy.**—The bones are thickened, rough, and for a long time softer than normal. The long bones are more or less cylindric and abnormally curved. Internally, the ordinary relation of compact and cancellated structure is destroyed and in the long bones the marrow cavity is partially or completely obliterated. The superadded bone upon which the enlargement depends varies in appearance according to the stage of the disease. It may be fibrous and elastic, or, if calcification has occurred, partly trabecular and partly dense and ivory-like. The process is apparently a dual one, consisting of resorption of normal bone and excessive regeneration, the new bone tissue, which springs from both the periosteum and the marrow, remaining uncalcified for a long time, so that deformities ensue.

**Symptoms.**—The process usually begins in the tibiæ or calvarium, and always develops insidiously. In many cases the first symptom to attract attention is the increase in the size of the head, the loss of stature or the pronounced bowing of the legs. When the disease is well developed the appearance is characteristic. The head is enormously enlarged, irregularly oval-shaped, with the broad end up. The spine is curved forward, and the chest in consequence is sunken toward the pelvis. The abdomen is small and protruding and usually with a deep transverse sulcus. Owing to the forward position of the trunk, the arms appear unusually long and ape-like. They are often also abnormally curved. The pelvis is broad, the legs are bowed outward and forward, and the feet are everted. The gait is stiff and "waddling," but usually there is no actual arthritis. In addition to these distortions the affected bones are uneven and remarkably massive. Although multiplicity of the bones involved has been regarded as a constant characteristic, a few instances of *mono-osteitic* Paget's disease have been reported. X-ray studies are of great value in confirming the diagnosis. They show that the process affects the entire bone, and that with rare exceptions it begins simultaneously in several bones. They also reveal clearly the enormous thickening, the loss of normal markings, the encroachment upon the marrow cavity, and the irregular distribution of calcium deposits.

Subjective symptoms are not always present, but pains in the limbs, usually referred to as rheumatic, and cramps in the muscles of the legs are

[1] Amer. Jour. Med. Sci., June, 1916.
[2] Med.-Chir. Trans., vol. lx, 1877.

very common. Arteriosclerosis develops early and is often pronounced, the general health is usually more or less impaired, and signs of senility appear prematurely. Insanity has been recorded in a few instances. Malignant disease of the bones or other tissues is a somewhat frequent association. In 158 cases analyzed by Higbee and Ellis[1] there were 14 instances of tumor growth. As the new osseous tissue is fairly elastic, fractures are not common, but they may occur. The *course* of the disease is a long one, ranging from 10 to 40 years. A spontaneous arrest of the process is sometimes observed. Death results from intercurrent disease.

**Diagnosis.**—This is not often difficult. *Syphilitic periosteitis* affects, as a rule, only a portion of one bone, and does not completely disorganize the bony architecture; it is usually associated with other indications of syphilis, and responds favorably to antiluetic treatment. In *secondary hypertrophic osteoarthropathy* the fingers and toes are clubbed, and, if the large bones are affected at all, the process is limited to the distal ends of the forearm and leg bones and does not result in arching. *Osteomalacia* commonly affects young women, especially after child-birth; it does not cause hypertrophy of the bones, and rarely affects the skull. *Osteitis fibrosa cystica* occurs chiefly in children, rarely developing after the fortieth year, results in tumor-like enlargements (cystomas) of the bones, and shows a decided tendency to spontaneous fracture. In *acromegaly* the bones of the face are involved rather than those of the cranium, the soft parts, especially those of the face, hands and feet share in the hyperplasia, and there is no bending of the long bones. *Leontiasis ossea* (*cranial hyperostosis*), which is characterized by great thickening of the cranium, often with hard, tumor-like hyperostoses, giving the patient a leonine appearance, is probably a form of Paget's disease. It is peculiar, however, in not affecting other parts of the skeleton and in being frequently accompanied by neuralgia, facial palsies, blindness, deafness, etc., as a result of compression of the nerves in the foramina.

**Treatment.**—No known treatment is of any avail.

## OSTEITIS FIBROSA CYSTICA

### (Tumor-building Osteitis Deformans)

This rare disease, described by von Recklinghausen[2] in 1891, is characterized by resorption of bone and replacement of the osseous tissue by cellular fibrous tissue, which tends to soften and form multiple cysts. Not infrequently giant-cell sarcomas of slight malignancy develop in the cysts. As a result of the changes, the bones, especially the long bones of the limbs, the jaws and the skull, become brittle, thickened, and the seat of multiple tumor-like enlargements. The disease differs from osteitis deformans, to which von Recklinghausen believed it to be closely allied, in occurring chiefly in young persons (70 per cent before the twentieth year and 85 per cent. before the thirty-fifth year), in affecting females much more frequently than males, in producing well-defined cystomas, which are readily revealed by the x-ray, and in showing a marked tendency to spontaneous fracture. Cystic fibrous osteitis is incurable. It pursues a long course, and even when the process becomes sarcomatous metastasis does not occur.

[1] Jour. Med. Research, 1911, xxiv, No. 1.
[2] Fest. f. Virchow, 1891.

## ACHONDROPLASIA

(Chondrodystrophia Fetalis)

Achondroplasia is a dystrophic condition of the cartilaginous portion of the skeleton, occurring in intrauterine life and leading to permanent shortening of the limbs and dwarfism. Pathologically, the important features are (1) an interference with the normal row formation of the proliferating cartilage cells of the epiphysis, causing an arrest of growth in the length of the diaphysis, and (2) an ingrowth of the periosteum between the epiphysis and diaphysis, which also interferes with the growth of the bone in length and at the same time favors the development of curvatures. Despite the inhibition of endochondral ossification, calcification and periosteal bone formation proceed normally. The cause of the chondral abnormalities is obscure. According to Jansen[1] they are due to excessive infolding of the embryo and enhanced amnionic pressure, and are most marked in those parts of the skeleton which are latest formed and most immature at the time of injury.

Clinically, the chief characteristics of achondroplasia are: Dwarfism, with the trunk of normal size and the limbs disproportionately short and bowed; an abnormally large cranial vault, with a relatively small face, depression of the root of the nose, "pug-nose," and prognathus, these features being due to premature synostosis of the occipital and sphenoid bones; lumbar lordosis with a protuberant abdomen and prominent buttocks; short and broad hands, with fingers of equal length and tending to separate from one another at the level of the middle phalangeal joints, forming the so-called *main en trident* of Marie; a small and narrow pelvis, which in the female renders labor difficult or impossible; and normal mentality, walking, teething, and sexual development. Less frequent associations are a superabundance of subcutaneous fat, a high-arched palate, umbilical or inguinal hernia, and hydrocephalus. Many achondroplasics are stillborn or die in early childhood, but a fairly large proportion reach maturity. The condition is not amenable to any known treatment.

The diagnosis is rarely difficult and can always be made with certainty by the x-ray. The differentiation from *rickets* is considered on p. 344. In *cretinism* there is mental feebleness or actual idiocy, the skin is thick, wrinkled and dry, fatty pads occur in the supraclavicular fossæ, the tongue is large, salivation is usual, the sexual organs are small, the radiograph shows only stunted growth of the bones, and marked improvement occurs under the use of thyroid extract.

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## OSTEOGENESIS IMPERFECTA

(Idiopathic Fragilitas Ossium; Idiopathic Osteopsathyrosis)

Osteogenesis imperfecta is a comparatively rare condition in which multiple fractures occur during intrauterine life or infancy as a result of imperfect development of the bones. In many cases the child is born dead or dies in the first few weeks of life. In some instances, however, the patient survives and fractures continue to occur, either spontaneously or from trivial injuries, until puberty or even until adult life. The number of fractures varies from three or four to a hundred or more. Not rarely the skull is imperfectly ossified and the bones show, in addition to deformities due to improperly-united fractures, more or less curving and bending. A peculiar

[1] Jansen, Murk: Achondroplasia, Its Nature and Its Causes, Leyden, 1912.

blueness of the sclera is sometimes observed (Stephenson, Burrows, Rolleston, Cockayne, Bolten). With the roentgen ray the bones appear thin and atrophic, and the medullary cavity is constantly increased in size, but the epiphyseal lines are clearly defined. The prognosis is usually unfavorable, about one-half of the survivors remaining badly crippled. The etiology of the disease is unknown. An inherited or a family predisposition, however, is not rarely found. The diagnosis is, as a rule, not difficult and should exclude *symptomatic osteopsathyrosis*, or excessive brittleness of the bones from recognizable causes, such as that due to osteomalacia, fibrous osteitis, rickets, senile osteoporosis, inflammatory osteoporosis (osteomyelitis, syphilis, etc.), neurotic atrophy (tabes dorsalis syringomyelia, paretic dementia), or tumors of bone. Cases of so-called "congenital rickets" and so-called "juvenile osteomalacia" are in many instances examples of osteogenesis imperfecta. No satisfactory treatment of the condition has been found.[1]

## OSTEOMALACIA

**(Mollities Ossium)**

Osteomalacia is a chronic disease of adults affecting the bones, characterized by decalcification and the formation of new osteoid tissue which remains uncalcified, and manifested clinically by rheumatoid pains, various skeletal deformities, infractions, and fractures.

**Etiology.**—The disease is relatively common in certain parts of Germany, Switzerland and Northern Italy, but it is rare in Great Britain and in the United States. In about 90 per cent. of the cases the patients are women and in more than 80 per cent. women who have borne children, the condition coming on during pregnancy or lactation, often disappearing after the suspension of lactation, and returning with subsequent pregnancies. Childless women are affected about as frequently as males. A senile form is occasionally observed. In a few instances generalized osteomalacia has followed local trauma. The cause of the decalcification is not known. Some functional disturbance of the ductless glands, especially the ovaries, has been suggested.

**Morbid Anatomy.**—The bones most commonly affected are the pelvic bones, the vertebræ and the ribs. The long bones usually are affected late, especially in puerperal cases, and the cranial bones in most cases escape. The lesion consists in decalcification of the original bone and a more or less extensive formation of new osteoid tissue, which for a time, at least remains uncalcified. The process is similar to that occurring in rickets, but in the latter the decalcification is not progressive and a failure on the part of the *normal* osteoid tissues to take the calcium from the blood is an important feature. The changes in the bones explain the striking deformities and the tendency to fractures that characterize the disease.

**Symptoms.**—Osteomalacia usually develops insidiously and often fails of recognition until after the occurrence of deformities. Dull pains in the back, thorax, pelvis, or legs, aggravated by movement and by pressure, are in most cases, however, the earliest manifestations. Accompanying the pains there is frequently a sense of weakness and a tendency to spasm of the

[1] For a more full account of the disease the reader is referred to the following papers: Griffith, Amer. Jour. Med. Sci., 1897, cxiii, 426; Lovett and Nichols, Brit. Med. Jour., Oct. 3, 1906; Niklas, Ziegler's Beiträge, 1915, lxi, 101.

muscles, the gait in consequence becoming uncertain and hobbling. Gradually deformities ensue. In child-bearing women the pelvis is especially affected and eventually the distortions become so pronounced that parturition is greatly impeded or is even rendered impossible. As the disease progresses the vertebræ, ribs and long bones yield to the weight of the body and the action of muscles, the results being lordosis or other curvature of the spine, flattening of the chest, curving of the legs, and a progressive reduction of the patient's stature. Finally, dyspnea develops as a consequence of the thoracic deformity and costal pains, the muscles waste and display fibrillary twitchings, the general nutrition becomes impaired, and the patient lapses into a condition of helpless invalidism. The urine and feces often show excessive amounts of calcium and phosphates. Roentgen ray examination of the affected bones shows thinning of the cortex and diffuse rarefaction. Renal calculus is an occasional complication.

The tendency of osteomalacia is to continue for years, with remissions and exacerbations, the latter in women occurring with pregnancy, sometimes with menstruation. Recovery or arrest of the process frequently occurs, however, either under appropriate treatment or spontaneously.

**Diagnosis.**—The diagnosis is often difficult until the skeletal changes are well developed. The disease at first may be confused with certain nervous affections, such as hysteria, tabes and polyneuritis, and later with multiple myeloma, idiopathic fragilitas ossium, osteitis deformans and generalized fibrous osteitis. *Multiple myeloma* occurs chiefly in males, its course is that of a malignant tumor, and it is usually associated with Bence-Jones proteinuria. *Idiopathic fragilitas ossium* often results in spontaneous bending and curving of the bones, but this disease occurs chiefly in infancy or childhood, is often hereditary or familial, and is characterized by recurring fractures from trivial injuries or without obvious cause. The differentiation of *osteitis deformans* is considered on p. 881. *Generalized fibrous osteitis* can probably not be definitely excluded in all cases. However, this disease occurs chiefly in children, and is characterized by definite cyst formation, which when well developed results in multiple tumor-like enlargements of the bones.

**Treatment.**—A good hygienic environment, an abundant nutritious diet, the termination of lactation, and the avoidance of pregnancy are important indications. Medicinal treatment is empiric. Phosphorus and epinephrin have been efficacious in some cases. Phosphorus is best given in pill form and in doses of $\frac{1}{100}$ gr. (0.00065 gm.) three times a day, over several months. Epinephrin is given subcutaneously in doses of 0.5 to 1.0 mil of the 1:1000 solution, once daily, for three or four months. Castration, originally suggested by Porro, has many successes to its credit, and is advisable when other measures fail. Whether it acts by removing some baneful influence of the ovaries themselves or solely by the prevention of pregnancy is debatable. According to Schnell[1] recovery occurred in 98 of 105 cases treated by castration and in 12 of 32 cases treated by epinephrin. Sterilization by roentgen rays has proved beneficial.

[1] Ztschr. f. Geburtsh. u. Gynäk, lxxv, No. 1, 1913.

# Diseases of the Muscles and Myopathies without Obvious Changes in the Nervous System

## MYALGIA

Myalgia is a comparatively frequent condition affecting individual muscles or groups of muscles and characterized by varying degrees of pain and at times more or less stiffness and disability. The pain, which is the chief symptom, is usually increased by movement, and in consequence the affected muscles are in many cases instinctively held in certain positions to avoid contractions. The nature of the process is not well understood. Although the term "muscular rheumatism" has been applied to the condition, it is now generally recognized that only a very small proportion of cases are of rheumatic origin. It is probable that in some instances, as Senator maintained, there is a slight neuritis affecting the intramuscular sensory nerves, and in others a mild form of myositis, although the phenomena of inflammation, other than pain, are usually wanting. In a third group of cases, and by far the largest group, the pain is not caused by changes in the affected muscles themselves, but is merely referred to the muscles from lesions in other structures.

The **causes** of myalgia differ in the acute and chronic forms. The acute forms are frequently due to chilling of the body, especially during perspiration. Strains and over-use of the muscles are responsible for some cases. The myalgia accompanying the acute infections, such as rheumatism, influenza, typhoid, smallpox, tonsillitis, etc., is well known, and is doubtless due to the absorption of toxins. The causes of the more chronic forms of myalgia are varied and include (1) various chronic intoxications, such as may result from alcohol, lead, diabetes, gout, etc.; (2) chronic infections, such as syphilis tuberculosis, and focal septic infection; (3) unusual strain from a lack of muscular balance; and (4) lesions of the joints, bones, and viscera, the nerves of which are in relation with those of the affected muscles.

Common types of myalgia are: *Torticollis* (stiffneck), in which the sternomastoid and sometimes the trapezius are the seat of the pain. The affected muscles are stiff and fixed, and great pain is experienced on attempting to turn the head in the opposite direction. *Pleurodynia* affects the muscles of the chest, usually the intercostals. The pain, which is often severe, is increased by all movements of this region, such as occur in deep breathing, coughing, sneezing, etc. The condition simulates pleurisy and intercostal neuralgia, but in the former there are usually characteristic physical signs, and in the latter the pain is paroxysmal and along the course of the intercostal nerves, and *pointes douloureux* can usually be detected. *Lumbago* affects the muscles of the lumbar region. As it is such a common condition it is described separately.

The **duration** of myalgia is exceedingly variable. Acute cases last usually from a few days to a week or two; but chronic cases often continue with remissions or intermissions for many months or years. Persistent

fixation of the muscles sometimes results in actual contractures. The treatment is considered under Lumbago.

## LUMBAGO

### (Backache)

Acute lumbago usually is due either to chilling of the body or to strain of the lumbar muscles. Gout is believed to favor its occurrence. It is observed most often in men and in adult life. The pain frequently comes on suddenly and may be dull or sharp and lancinating. It is always increased by movement, being especially severe when the patient rises to the erect posture after sitting or stooping. The more chronic forms of lumbago may be due to the following conditions: (1) Defective muscular balance. This may be the result of a faulty posture, spinal deformity, shortening of one leg, flat foot or abnormal conditions in the abdomen. (2) Lesions of the spine or sacro-iliac joints. Under this head are included osteo-arthritis of the spine, infection of the vertebræ from syphilis or tuberculosis, new growths, osteomalacia, and strains, relaxation and infection of the sacro-iliac articulations. (3) Traumatism. This may be direct or indirect and result in arthritis or sprain. The damage may be done in lifting heavy objects, in vaulting, in sitting down precipitately, or even in long-continued lying on the back. (4) Abnormal conditions within the abdomen, such as enlargement of the organs, visceroptosis, renal calculus, abdominal obesity, etc. In some of these cases the pain is a "referred sensation" and in others it is probably the expression of muscular fatigue induced by defective balance. (5) Abnormal pelvic conditions. Retroversion of the uterus, prolapse of the uterus, diseases of the ovaries, prostatitis, cancer of the prostate, rectal carcinoma, etc., are common causes of backache. (6) Chronic infections. Septic infection in the tonsils, teeth sockets, urethra, etc. frequently results in lumbago by setting up osteo-arthritis of the spine or possibly in some instances an independent myositis. (7) Chronic intoxications due to alcohol, lead, etc., and obscure toxemias resulting from disordered metabolism. (8) Neurasthenia and hysteria. Lumbago often occurs in neurasthenia as one of the localized sensations of fatigue and in hysteria ("traumatic neuroses") as a symptom produced by suggestion.

The pain of chronic lumbago varies considerably in degree. It may be merely a crick in the back on exertion or a dull ache, or it may be so severe as to prevent any movement. In some cases, especially in those due to arthritis, it radiates over the buttocks and down the backs of the thighs. Tenderness is often present over the lumbar spine or sacro-iliac joints. The etiologic factor must be determined in each case from the history and the results of a thorough physical examination. The roentgen ray is often a valuable aid.

The **treatment** varies with the cause. In acute cases anodynes are required. A combination of aspirin and phenacetin often suffices. Occasionally it may be necessary to resort to morphin. Locally, heat, support by straps, friction with methyl salicylate or irritating liniments, or dry cupping almost always affords great comfort. An excellent method in many cases is to rub the part thoroughly with methyl salicylate, cover it with flannel, and then pass over it several times a heated flat-iron. In obstinate cases mustard plasters, flying blisters, or light applications of the Paquelin cautery should be tried. Free sweating is sometimes useful. In chronic lumbago treatment must be addressed to the underlying condition. Cases due to sprain, arthritis or sacro-iliac relaxation will require immobiliza-

tion of the parts by straps of adhesive plaster or specially constructed corsets. Unilateral defects in balance are sometimes corrected by elevating one heel. Lumbago due to a pendent abdomen is usually relieved by a close-fitting supporter or corset. In septic cases the primary source of the infection must be removed. Backache resulting from relaxed muscles and postural curve will be benefited by the assumption of a correct standing and sitting position, gymnastic exercises, massage, shoulder-straps, etc. In severe cases, irrespective of the cause, recumbency for a part of the day is often necessary at first.

## MYOSITIS

Myositis is usually the result of trauma or of the direct extension of inflammatory processes in the joints, bones, skin, mucous membranes, etc. Hematogenous and lymphogenous forms, however, occur in general infections, such as pyemia, typhoid fever, tuberculosis, glanders, etc. and in association with focal septic infection in the tonsils, teeth, genito-urinary tract, etc. Chronic interstitial myositis (fibrous myositis) also occurs in spinal and myopathic atrophy, in persistent local anemia (Volkmann's contracture) and around foreign bodies, parasites, etc. Acute myositis may be simple or suppurative. The latter arises from infected wounds, purulent arthritis, skin-phlegmons, etc. or occurs in the course of pyemia, glanders, etc. Two peculiar forms of myositis merit separate consideration, namely, acute polymyositis and myositis ossificans.

### ACUTE POLYMYOSITIS (DERMATOMYOSITIS)

This rare condition, described independently by Unverricht, Hepp and Wagner[1] in 1887, is characterized by widespread painful swellings of the muscles, different parts of the body being affected progressively or in intermittent attacks. An extensive edema of the subcutaneous tissue usually accompanies the myositis, and an erythematous rash, commonly diffuse but occasionally macular, is frequently present. The limbs suffer most, and then in order, the muscles of the chest, abdomen, face, and neck. The temperature is raised, the spleen is often enlarged, and not rarely there is free hyperhidrosis. Stomatitis and angina are sometimes observed. The disease lasts from a few weeks to a year or more.

The *prognosis* of polymyositis is doubtful, although mild cases often terminate favorably. Death may occur from involvement of the muscles of deglutition and aspiration pneumonia, from exhaustion, or from nephritis. In the more chronic cases permanent muscular atrophy and a scleroderma-like condition may supervene. In the **diagnosis,** polyneuritis and trichiniasis may cause confusion, but in the former the tenderness is mainly over the nerve-trunks, inflammatory edema is rarely marked, and paresthesia or anesthesia is an important feature; while in the latter there is usually a history of raw pork having been eaten and of prodromal intestinal symptoms, eosinophilia is almost constantly present, and the trichinæ may be found in pieces of excised muscle. **Treatment** in the early stages consists in the administration of sedatives (aspirin, phenacetin, morphin, etc.) and the systematic employment of diaphoretic measures. During convalescence massage and electricity may be of service.

[1] Arch. f. klin. Med., 1887, xl, 241.

### MYOSITIS OSSIFICANS

Myositis ossificans is an affection characterized by the formation of bone in or between the muscles. There are two forms, the traumatic and the progressive. **Traumatic myositis ossificans** is limited to one muscle or a group of muscles. It results from a single severe contusion or, more frequently, from long-continued irritation. The muscles most frequently involved are the deltoid (exercise-bone) and the adductors of the thigh (rider's bone). The newly formed osseous material may be attached to an adjacent bone or occur as a movable mass in the muscle. **Progressive myositis ossificans** is a rare condition in which ossification successively occurs in many parts of the muscular system. The disease usually begins in youth and attacks first the muscles of the back and neck. The formation of bone is preceded by painful swellings. In the end there may be almost complete loss of function with rigid fixation of the body. The etiology is unknown. A congenital disturbance of the osteoblastic tissue has been suggested, and this theory receives some support from the association of microdactylism in about 75 per cent. of the cases.[1] Traumatism sometimes determines the site of the lesions.

## PROGRESSIVE MUSCULAR DYSTROPHY

**(Primary Myopathy)**

**Definition.**—Progressive muscular dystrophy is a gradual wasting of the muscles occurring independently of any demonstrable lesion in the nervous system and apparently the result of an inherent defect in the muscles themselves.

**Etiology.**—The actual cause of the condition is unknown. In the majority of cases, however, a distinct hereditary predisposition is present, and very often several members of one family are attacked. Males more frequently suffer than females, although the transmission is more likely to occur through the mother than the father. With rare exceptions the atrophy makes its appearance in childhood or early youth. In some cases exposure to cold, overexertion, traumatism, or an acute infection, such as typhoid fever or measles, seems to stand in causal relation to the disease, but in how far these factors are really operative is an open question.

As regards the pathogenesis of the myopathies, it has been maintained by some authorities that there is a premature death of the muscle fibers as a result of a congenital defect of vital endurance (abiotrophy). According to another hypothesis the basic condition is a disturbance of the glands of internal secretion.

**Morbid Anatomy.**—Microscopic examination of the muscle fibers shows simple atrophy, nuclear proliferation, vacuolation, and segmentation. A true hypertrophy of individual fibers is sometimes seen. The spaces between the wasted fibers are occupied by proliferated connective tissue and an excessive deposit of fat cells. In certain parts the replacing lipomatosis may be so pronounced that the volume of the whole muscle is increased rather than decreased, muscular pseudohypertrophy resulting. Atrophy of the bones has been observed in a few cases. No constant lesions have been found in the nervous system.

**Symptoms.**—Muscular atrophy beginning first, as a rule, in the trunk or

[1] De Witt, Amer. Jour. Med. Sci., Sept., 1900.

proximal parts of the limbs, and slowly spreading from one region to another; diminution and eventually abolition of the tendon reflexes; and lessened electrical excitability in the wasted muscles, without, however, reaction of degeneration, are the chief features. Fibrillary tremors are nearly always absent, the sphincters are intact throughout, sensation is unaffected, and the mentality, although it may be somewhat deficient, is not markedly impaired. In 9 cases studied by Janney, Isaacson and Goodhart[1] metabolic changes suggestive of endocrine origin were found, namely, hypoglycemia, low values of creatinin in the blood, and abnormal presence of creatin in the urine.

Several varieties of the disease have been described—*pseudohypertrophic, scapulo-humeral* or *juvenile,* and *facio-scapulo-humeral*—in accordance with the presence or absence of enlargement of any of the affected muscles, and the time of the appearance and the primary localization of the atrophy, but there is no hard and fast line between one type and another. Mixed and transitional cases are frequently observed and not rarely two or even three forms are observed among members of the same family.

**Pseudohypertrophic Type.**—This type usually begins before the tenth year and attacks first the muscles of the lower extremities. Awkwardness in using the legs and a tendency to stumble are, as a rule, the earliest indications. Sooner or later certain muscles, usually those of the calves, show an increase of volume, which is strangely at variance with their decreasing strength. Other muscles, especially those of the thighs, buttocks, and back may undergo a similar change and occasionally those of the shoulders are also attacked. In the majority of cases, however, the muscles of the calves are the only ones enlarged, those of the rest of the body retaining their normal bulk or shrinking. Ultimately, even the hypertrophied muscles may decrease in volume and become atrophic.

Owing to the weakness of the muscles involved, the child's attitude in standing, his gait, and his mode of rising from a recumbent position are almost characteristic. He stands with the feet far apart and the shoulders thrown back, sometimes beyond the buttocks, the lumbar concavity being correspondingly exaggerated. In walking, on account of the weakness of the glutei, he raises the pelvis abnormally high and thus sways the body from side to side, after the manner of a duck in waddling. In rising from the floor, the patient, as it were, climbs up his own legs, that is to say, he turns over on "all fours," raises the trunk by means of the outstretched arms, and then works the hands backward to the legs, grasping the latter at higher and higher levels, until at last he forces the body into an erect position.

Late in the disease contractures occur, causing various deformities.

**Scapulo-humeral or Juvenile Type (Erb).**—This form usually appears about puberty, but it may not develop until adult life.. The atrophy begins in the muscles of the shoulder girdles and then spreads to those of the arms, back, and lower extremities. The muscles of the forearms and hands usually remain normal.

**Facio-scapulo-humeral Type (Landouzy-Déjérine).**—In this type, which usually develops in early childhood, the muscles of the face, especially those about the mouth are first attacked. The face is expressionless, the mouth cannot be completely closed, and the lips protrude, producing the so-called "tapir mouth." Later, the muscles of the neck, arms, trunk, and lower extremities become involved as in the juvenile type of Erb.

**Course.**—The course of the disease is progressive, the atrophy slowly extending from muscle to muscle, until finally the patient becomes bedridden

[1] Arch. Intern. Med., Feb., 1918.

and helpless. Occasionally nearly every voluntary muscle in the body is involved. The duration varies from a few years to several decades. Death usually results from some intercurrent disease and most frequently from pneumonia.

**Diagnosis.**—Primary myopathies are not likely to be confused with other diseases. In *spinal progressive muscular atrophy* the distal ends of the extremities are usually first affected, fibrillary tremors are present, and the wasted muscles yield the electrical reactions of degeneration. *Neural muscular atrophy* also shows a preference for the distal parts of the limbs and is accompanied by sensory disturbances. *Syringomyelia* very rarely attacks first the proximal arm muscles and shoulder-girdle and is always attended with disturbances in sensation. *Amyotonia congenita* (myatonia congenita) may be recognized by its congenital origin, the extreme flaccidity of the muscles without appreciable atrophy, and the absence of any tendency in the paralysis to spread.

**Treatment.**—Avoidance of fatigue, hydrotherapy, massage, electric procedures, and the administration of tonics, especially strychnin, may retard the progress of the disease but never arrest it. Extracts of the adrenal, pituitary, and thymus glands seem to have been of service in some cases.

## MYOTONIA CONGENITA

### (Thomsen's Disease)

This comparatively rare condition, first accurately described by Thomsen,[1] is characterized by tonic contraction or rigidity of the muscles upon attempted motion. In the vast majority of cases it is hereditary and familial. Thomsen reported that in his own family in five generations more than 20 persons suffered from it. Although the disease is usually congenital it frequently passes unnoted until puberty or early manhood. Males are much more frequently attacked than females.

When the affected muscles are put into action a painless tonic spasm occurs, which either greatly impedes the movement or completely inhibits it. With repeated attempts to overcome the resistance, the spasm disappears and does not return while the same muscles are being used. The disturbance always returns, however, after an interval of rest. Cold, dampness, excitement, and fatigue aggravate the condition, whereas warmth, light muscular exercise, and agreeable mental effort have a favorable effect. The muscles of the extremities are chiefly involved, rarely those of the trunk, and still more rarely those of the lower jaw, eyes, tongue and larynx. The sphincters are never involved. When the legs are affected the myotonic disturbance is especially noted in walking. The first few steps are awkward and laborious, but with repeated attempts the gait gradually improves and in the course of a few minutes it becomes quite normal. When the hands are affected difficulty is experienced in extending the fingers after they have been brought into flexion.

The excitability of the muscles to mechanical and electrical stimulation is increased. Percussion produces a sharp contraction, often with the formation of a distinct groove lasting 5 to 20 seconds. Both the faradic and the galvanic current produce contractions which last longer than in health. In the case of the galvanic current AnClC is equal to or greater than CaClC,

[1] Arch. f. Psych. u. Nervenkrankh., 1876, vi, 3.

and with the stabile application wave-like contractions may occasionally be seen passing from the negative to the positive pole. These electrical changes constitute the myotonic reaction of Erb.[1] The affected muscles are usually plump and may be considerably enlarged, but the strength of the contractions is less than normal; moreover muscles that give a typical myotonic contraction on voluntary effort respond normally when brought into activity by reflex stimulation (Johnson and Marshall[2]). Occasionally myotonia is associated with wasting of the muscles (*amyotrophic myotonia*), and in this case the myotonic reaction is modified.

The nature of Thomsen's disease is obscure. Histologic examination of the muscles shows pronounced enlargement of the fibers, as a result of an increase in the number of fibrils, but no relative increase in the nuclei or variations in striation. The muscle changes are probably secondary effects and the result of some disturbance in the corticospinal motor paths. Johnson and Marshall suggest that there is an increased resistance to the passage of nervous impulses, the partial block probably being in the synapses, for strychnin, which is known to facilitate the passage of impulses from one neuron to another, temporarily abolishes the obstruction. The affection does not shorten life, but there is no prospect of recovery, and **treatment** is almost powerless. Massage and light gymnastics are recommended. The experimental researches of Johnson and Marshall suggest that strychnin may prove useful.

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## MYATONIA CONGENITA

**(Amyotonia Congenita; Oppenheim's Disease)**

This rare disease of early childhood, to which Oppenheim[3] first drew attention, is characterized by a more or less extensive flaccid paralysis, with partial or complete loss of the tendon reflexes and diminished electrical contractility. It is probably always congenital, although it not rarely fails of recognition until the age is reached when the child is expected to walk or to use its arms. The muscles of the limbs, trunk and neck may all be affected, but in most of the cases only the limbs are involved. The legs suffer more than the arms and the proximal parts more than the distal. The muscles of bulbar innervation are rarely, if ever, affected. The sphincters are always intact. The loss of power varies from pronounced weakness to almost complete paralysis. In severe cases walking, standing and even sitting are impossible, the legs are limp and inert, and the head falls loosely in any direction. The affected muscles are soft and flabby, but apparently not atrophied; the joints are abnormally movable; the electrical response is diminished or absent, but never qualitatively altered; and the tendon reflexes are weak or abolished. Sensation and intelligence are undisturbed.

The nature of the disease is obscure. In some cases the only pathologic findings have been in the muscles and have consisted of attenuation of the fibers, increase of nuclei, and overgrowth of connective tissue; but in other cases abnormalities (scarcity and imperfect development of the cells of the anterior horns) have been observed in the spinal cord. Whether the process is one of retarded muscular development, as Oppenheim thought, or of congenitally enfeebled ganglion cells (abiotrophy) with secondary changes

[1] Erb, Die Thomsensche Krankheit, 1886.
[2] Quart. Jour. Med., 1915, viii, 114.
[3] Monatsschr. f. Psychiat. u. Neurol., 1900, viii, 3.

in the muscles, it is as yet impossible to say. When the symptom-complex is typical the diagnosis is easy. The *muscular dystrophies* are usually hereditary or familial and are never congenital. They are marked by a considerable degree of atrophy or pseudo-hypertrophy, and are always progressive. *Infantile spinal progressive muscular atrophy* (*Werdnig-Hoffmann* type) is also strongly hereditary and familial. It attacks first the muscles of the pelvic girdle and thighs, produces conspicuous atrophy, and is eminently progressive. *Acute poliomyelitis* may be distinguished by the history of the onset, and by the occurrence of wasting and of the reaction of degeneration in the paralyzed muscles. In the pseudoparalysis of *hereditary syphilis*, of *infantile scurvy*, and of *rickets* there is generally other evidence of the constitutional malady, the limbs only are involved, tenderness is present, and passive movement is usually productive of spasm. The outlook in myatonia is fairly good for improvement, but not for complete restoration of power. In 11 of the recorded cases death occurred at an early age from pneumonia (Haberman[1]). Massage, electricity and passive gymnastic exercises are the therapeutic measures to be employed.

## MYASTHENIA GRAVIS

**(Asthenic Bulbar Paralysis)**

This comparatively rare disease, first described by Wilkes[2] in 1877, is characterized by gradually developing muscular weakness, which is peculiar, in that it affects first and most strikingly the muscles of bulbar innervation and is subject throughout to marked variations in intensity, being much worse after exertion and decreasing or even disappearing for a time under rest.

The disease usually appears between the ages of twelve and fifty years and shows a slight preference for the female sex. In many cases it has followed some acute illness or the puerperal state. At autopsy the most constant finding has been the presence of foci of lymphocytes, with varying numbers of mast cells and plasma cells among the muscle fibers, the latter themselves not being invaded and rarely showing any degenerative changes. According to W. A. Jones,[3] 27 of 56 necropsies recorded since 1901 showed persistence, hyperplasia or actual tumor (usually thymoma) of the thymus. Von Ketly[4] concludes from a study of 134 cases, with 42 necropsies, collected from the literature that the nervous system is intact. As regards pathogenesis, the two most plausible views are that myasthenia gravis is a disturbance of muscular metabolism *per se*, or an autointoxication resulting from defective functioning on the part of the ductless glands.

The onset is usually gradual. Ptosis, of varying intensity, generally bilateral and more marked on one side than on the other, is one of the earliest and most constant signs. Weakness of the orbital muscles causing diplopia, strabismus, or even complete ophthalmoplegia externa is often noted. Pupillary changes, however, are extremely rare. Occasionally, diplopia precedes the other symptoms by several years. The muscles of the face, jaw, soft palate and pharynx are frequently implicated, so that inability to whistle, immobility of the angles of the mouth in smiling ("nasal smile"), difficulty

[1] Amer. Jour. Med. Sci., Mar., 1910.
[2] Guy's Hospital Reports, 1877.
[3] Jour. Amer. Med. Assoc., Nov. 4, 1916.
[4] Deutsch. Zeit. f. Nervenheilk, 1906, Bd. 31.

in mastication and swallowing, and impairment of articulation are common symptoms. In many cases the muscles of the neck, trunk, and limbs also suffer. Thus, the head may have a tendency to fall forward or backward, dyspnea may occur on the slightest exertion, and the arms and legs may become rapidly exhausted by exercise. The symptoms sometimes disappear entirely after a period of rest, as in the morning, but as a rule a variable degree of persistent paresis is found, especially in the muscles of the eye.

Another important phenomenon, usually but not invariably observed, is the so-called myasthenic reaction of Jolly.[1] When this is present the affected muscles are speedily exhausted by a tetanizing faradic current, but again respond after an interval of rest. Even after complete exhaustion by faradism the muscles still respond to the single shock of the galvanic current.

Neither muscular atrophy nor fibrillary twitching is observed, the tendon reflexes are usually active, sensation and intelligence are undisturbed, and the sphincters are always intact.

Various metabolic disturbances have been reported, the most common being the abnormal presence of creatin in the urine, low values of creatinin in the blood and urine, and some increase of the calcium output. A reduced metabolic rate and a low percentage of blood sugar have also been noted (Timme). Bronzing of the skin has occasionally been observed and in a few instances the disease has been associated with exophthalmic goiter.

The outlook is, as a rule, unfavorable. In most cases the disease runs a chronic course marked by many remissions and exacerbations, and terminates fatally from suffocation, either in a crisis of dyspnea or during the ingestion of food. The average duration of the fatal cases is about 1½ years. Actual recovery is probably rare, absence of symptoms, even for years, being usually followed by relapse. However, of 14 patients treated by Dana,[2] 5 lived more than 5 years, and in 3 cases the duration of the disease was from 12 to 17 years.

Myasthenia gravis may be distinguished from *progressive bulbar palsy* by the involvement of the ocular muscles, the myasthenic reaction, the absence of muscular atrophy and fibrillary tremors, and, above all, by the marked variation in the severity of the symptoms. In *pseudobulbar palsy* there is, as a rule, a history of apoplectiform attacks, the ocular muscles are rarely involved, spastic motor disturbances in the arms and legs are commonly present, intelligence is impaired and the characteristic remissions of myasthenia are absent. In *hysteria* ocular and facial palsies do not occur, although drooping of the eyelid from spasm of the orbicularis is occasionally observed; characteristic changes in the field of vision, however, are common; sensory disturbances are almost always present, and the myasthenic reaction is lacking. In *polioencephalitis superior* the onset is sudden and the symptoms do not remit. *Ophthmoplegic migraine* is associated with headache, spectral phenomena in the field of vision, mydriasis and impairment of accommodation. *Botulism* may be recognized by its occurrence in other persons who have partaken of the same food as the patient, by its acute onset, by the presence of pupillary changes, and, perhaps, by the appearance of vertigo, nausea and vomiting at the onset.

*Epidemic encephalitis* may simulate myasthenia gravis, but the differentiation can usually be made by the occurrence of similar cases in the community, by the associated cerebral disturbance (lethargy, apathy, somnolence, etc.), by the presence of fever, muscular pains, etc. at the onset, and by the absence of the peculiar myasthenic reaction. Finally, the distinct possibility of

[1] Berlin. klin. Woch., 1895, Bd. xxxii.
[2] Jour. Amer. Med. Assoc., Jan. 28, 1922.

confusing the ocular forms of myasthenia gravis with beginning *cerebral syphilis* or *tabes* must be mentioned.

Treatment is unsatisfactory. Rest of body and mind, careful feeding, and the avoidance of cold are of most importance. If the symptoms are severe the patient should be confined to bed. Electricity, especially, faradism, is contraindicated. Massage is useless. Strychnin has been employed, but not often with benefit, although Dana reports good results from the drug when given hypodermically in doses cautiously increased to ¼ grain (0.016 gm.) once a day or even twice a day. In individual cases improvement has followed the use of pituitary and ovarian extract (Delille and Vincent), adrenal extract (Sicard, Dufour), thymus extract (Goodhart), calcium actate (Spiller), and roentgen-ray treatment of the thymus (E. W. Taylor).

# DISEASES OF THE NERVOUS SYSTEM

## DISEASES OF THE MENINGES

### CEREBRAL PACHYMENINGITIS

Either layer of the dura mater may be the seat of inflammation and the process may be suppurative, productive, or hemorrhagic.

**Suppurative pachymeningitis** is usually the result of fracture of the cranium or of inflammation of the cranial bones arising from suppurative middle ear disease, syphilis or tuberculosis. When the process is diffuse the symptoms are similar to those of purulent leptomeningitis (*q. v.*). If the collection of pus is circumscribed, which is frequently the case, there may be focal symptoms referable to irritation or to compression of the cortex. The *treatment* is mainly surgical.

**Productive pachymeningitis** commonly develops slowly as the result of traumatism or syphilis. Occasionally, it is the sequel of acute pachymeningitis. The dura is thickened and firmly attached to the pia-arachnoid and to the inner surface of the calvarium. In many cases the bone itself is abnormally dense and heavy (*ossifying pachymeningitis*). The usual symptoms are persistent headache, often referable to a limited area, tenderness of the head on percussion, and incapacity for mental work. In some instances focal symptoms also appear. These usually take the form of Jacksonian epilepsy. The *treatment* must be based upon the cause. Iodids should be given a thorough trial, especially in syphilitic cases. Counter-irritation over the back of the neck by means of the Paquelin cautery is sometimes beneficial. The traumatic form is not rarely amenable to surgical operation.

**Hemorrhagic Pachymeningitis; Internal Pachymeningitis.**—This is a comparatively rare form of chronic pachymeningitis, affecting chiefly the inner layer of the dura and usually associated with more or less atrophy of the cerebral convolutions. It occurs more frequently in the aged than in the young and is most commonly met with in cases of chronic insanity, especially paretic dementia and senile dementia. It may occur, however, in chronic alcoholism, syphilis, severe anemia, tuberculosis and other wasting diseases, and occasionally it has been observed as a sequel of traumatism or sunstroke. Its occurrence in poorly nourished children has been noted by Doehle,[1] Northrup,[2] and others.

The disease is characterized by the formation, one after another, of delicate lamina of connective tissue, very rich in thin-walled vessels, from which the blood is prone to escape. The hemorrhages are usually small, but sometimes they are sufficiently large to produce distinct tumor-like masses or *hematomata*. In many cases degenerative changes are found in the cerebral cortex at points corresponding to the overlying effusions. The pathogenesis of the condition is obscure. The lesions are probably of inflammatory origin, although some pathologists believe that the primary

[1] Verhand. d. X. Internat. Cong., 1890, Bd. v.
[2] Jour. N. Y. Path. Soc., 1891, p. 59.

change is a degeneration of the blood vessels and that the hemorrhages precede the exudation.

The *symptoms* of hemorrhagic pachymeningitis are, as a rule, too ill-defined to afford a clue to the existence of the disease. Dull headache, mental hebetude and dizziness are commonly present, but are likely to be ascribed to the underlying affection, and it is only when there are repeated hemorrhages of considerable size with symptoms of irritation or compression of the cerebral cortex—severe headache, increasing somnolence, Jacksonian convulsions, apoplectiform attacks, unilateral rigidity, etc.—that the diagnosis is at all possible. The course of the disease is variable. In some cases it is very slow and marked by a number of apoplectiform attacks separated by intervals of fairly good health. On the other hand the first or second apoplec iform attack may prove fatal.

The *treatment* is largely that of the causal condition. At the time of the occurrence of a hematoma the treatment should be that of intracerebral hemorrhage. If the symptoms point unequivocally to focal irritation or compression of the cortex trephining and the evacuation of the clot may be considered.

## ACUTE CEREBRAL LEPTOMENINGITIS

**Etiology.**—Acute inflammation of the pia-arachnoid, currently known as acute meningitis, is usually excited by the diplococcus intracellularis meningitiditis, the pneumococcus, the tubercle bacillus, or the pyogenic cocci, but it may be caused by various other organisms, such as the typhoid bacillus, influenza bacillus, colon bacillus, pneumobacillus of Friedländer, bacillus of plague, Bacillus pyocyaneus, bacillus of anthrax, bacillus of glanders, or the actinomyces. The infection may reach the meninges through the blood, the lymphatics, an open wound or continuity of tissue. The natural cavities situated near the cranium, such as the nasal, pharyngeal, aural, etc., are common portals of invasion.

The disease may be primary or secondary. Under the primary form are included (1) all cases of *cerebrospinal fever*, both epidemic and sporadic, and (2) the exceptional cases of *pneumococcic meningitis* which are not associated with pneumonia or with any demonstrable focus of pneumococcic infection in the middle ear, accessory nasal sinuses, or elsewhere.

Secondary meningitis occurs in association with the following conditions:

1. *Tuberculosis.*—In children the primary focus of dissemination is most frequently a caseous bronchial or mesenteric lymph-node; in adults it is usually an old tuberculous lesion in the lungs, joints or bones. Although the process not rarely appears to be primary in the meninges, it is invariably secondary.

2. *Septic processes in the vicinity of the brain*, more particularly suppurative inflammation of the middle ear and accessory nasal sinuses.[1] These are important causes of secondary meningitis. One of the pyogenic organisms or the pneumococcus is usually the infective agent.

3. *Various acute infections*, such as pneumonia, septicemia, erysipelas, typhoid fever, influenza, scarlet fever, etc. Aufrecht found meningitis in 7 of 253 fatal cases of pneumonia and Pearce in 2 of 121. In septicemia it is somewhat more frequent. It was present in more than 10 per cent. of the 209cases of ulcerative endocarditis collected by Osler from the literature. In erysipelas the meninges are occasionally involved either through the blood or through contiguity of tissue. Symptoms of cerebral irritation—headache,

[1] St. Clair Thomson (Brit. Med. Jour., Sept. 29, 1906) has discussed at length the subject of disease of the brain and its membranes as a result of nasal suppuration.

delirium, rigidity of the neck, twitching of the muscles, inequality of the pupils, etc., occurring in the course of pneumonia, typhoid fever, influenza, scarlet fever, and other acute infections, are not usually due to a true meningitis, but to a less severe reaction of the leptomeninges to the specific bacteria or their toxins which has been designated *meningismus* or *serous meningitis* (Dupré[1]).

In 1907 Boidin and Weil[2] collected from the literature 9 cases of acute meningitis developing in the course of secondary syphilis and since then many other cases have been reported. Hutinel[3] and others cite instances of acute meningitis developing on the basis of inherited syphilis. Acute syphilitic meningitis is likely to be confused with tuberculous meningitis.

4. *Traumatism.*—In rare instances ordinary acute meningitis has followed an injury that has not been sufficient to produce any demonstrable lesion of the cranial bones or underlying soft structures.

5. *Chronic Wasting Diseases.*—Acute meningitis is occasionally the immediate cause of death in chronic affections of the heart, lungs or kidneys, arteriosclerosis, and diabetes. The inciting organism in this form of terminal infection is usually the Streptococcus hæmolyticus, pneumococcus or staphylococcus.

As the lesions and symptoms of cerebrospinal fever and of tuberculous meningitis have already been described, the statements that are made in the following paragraphs have reference especially to other forms of acute meningitis.

**Morbid Anatomy.**—The inflammation may involve the meninges over the entire brain or it may be confined to a certain area. In the tuberculous and epidemic forms and in meningitis of otitic origin the base of the brain is the part chiefly affected, while in other forms of the disease the most marked changes usually occur on the convexity. Fibrino-purulent exudate is seen in the subarachnoid space and the pia-arachnoid is hyperemic, swollen, and cloudy. When the process is very active, the exudate is so extensive that it obscures completely the cerebral convolutions, but in the milder types of the disease, it may appear only as yellowish-white lines in the sulci along the chief vessels. The inflammation frequently involves to a greater or less extent the meninges of the spinal cord, the substance of the brain and cord, and the cranial nerves. The ependyma is almost always affected, but distention of the ventricles is usually most marked in the tuberculous cases.

**Symptoms.**—The symptoms vary with the nature of the lesions, being pronounced in some cases and almost latent in others. Headache, sometimes excruciating, is usually an early symptom. In many cases it persists until consciousness is completely abolished. Other symptoms of irritation, such as restlessness, photophobia, cutaneous hyperesthesia, grinding of the teeth, trismus and twitching of the muscles, are frequently observed. Except in infants, general convulsions are not common. Vomiting is of frequent occurrence, especially in basilar meningitis. Rigidity of the neck muscles and retraction of the head are significant features, but they are not marked unless the spinal meninges share in the inflammatory process. Delirium may be present from the beginning. For a time it is likely to alternate with lucid intervals or with somnolence, and toward the end it is superseded by coma. The pupils are variable, although they are usually contracted at first, and dilated, unequal, and insensible in the later stages. Optic neuritis is rare,

[1] Dupré: Meningitis serosa, Cong. méd. de Lyon, 1904.
[2] Presse Médicale, 1907, xv, No. 85.
[3] Presse Médicale, 1918, xxvi, No. 23.

except in the basilar form. Focal paralyses, particularly strabismus and ptosis, may occur but they are less common than in cerebrospinal fever or tuberculous meningitis.

Kernig's sign, which consists in the inability to extend the leg on the thigh when the patient is lying on his back and his thigh is flexed to a right angle upon the trunk, is almost always present, but it may be observed in conditions other than meningitis. Brudzinski's[1] neck-phenomenon, that is, flexion of the lower extremities at the hip and knee when the neck is passively bent forward is rarely lacking and is usually absent in other conditions. Brudzinski's[2] "contra-lateral reflex," which consists in the drawing up of one leg when the other is passively flexed at the hip-joint is less constantly present. In children with tuberculous meningitis, less frequently with other forms of the disease, percussion over the parietal boss, while the stethoscope is placed over the forehead, yields a short, high pitched, almost tympanitic note, which diminishes in intensity as the stethoscope is approached by the percussing finger. This phenomenon (Macewen's sign) depends on increased intracranial tension. The tâche cérébrale, or the occurrence of persistent redness wherever the skin lightly stroked with the finger-nail, may be elicited in all forms of meningitis, but it is by no means pathognomonic.

Fluid obtained by lumbar puncture is usually in excess and under increased pressure. After the lapse of 24 or 36 hours, except in the tuberculous form, it is almost always turbid, and it may be actually purulent. The protein content is considerably increased, but the dextrose content is decreased, sometimes to the vanishing point. In meningitis due to the meningococcus, pneumococcus or streptococcus cytologic examination of the fluid reveals an excess of cells (200–10,000 per cubic millimeter) with predominance of the polymorphonuclear leucocytes. In tubercu ous meningitis pleocytosis is usually much less marked, and except in the earliest stages or in very acute cases there is a great preponderance of lymphocytes. Bacteriologic examination of the fluid is of great importance in revealing the specific cause of the meningitis.

The systemic disturbances occurring in acute meningitis vary considerably with the nature of the primary disease. The temperature is, as a rule, irregular and only moderately elevated. The pulse-rate is usually accelerated, although in some cases, even in the early stages, it is less than 70 per minute. Such infrequency, occurring with pyrexia, is significant. Rapid alterations in both the rate and volume of the pulse are prone to occur without obvious cause. The respiration, unaffected at first, often becomes embarrassed, irregular, and sighing at a later period. Cheyne-Stokes respiration or Biot's respiration[3] may be observed in meningitis from any cause, but it is most frequently noted in the tuberculous form. The bowels are, as a rule, constipated and the abdomen is often decidedly retracted or scaphoid. Emaciation may occur with remarkable rapidity.

**Diagnosis.**—Ordinarily, the symptoms are so expressive that the recognition of the disease is easy. There are cases, however, in which the manifestations are so indefinite that an error in diagnosis is pardonable. This may be true even of the cases associated with suppurative inflammation of the middle ear and accessory nasal sinuses. Again, during the progress of certain acute infections, notably pneumonia and typhoid fever, it is some-

[1] Arch. de méd. des enf., 1909, xii, 745.

[2] Wien. klin. Woch., 1908, xxi, 255.

[3] Rapid but equally deep respiratory movements in groups, separated by intervals of apnea lasting several seconds to half a minute or longer.

times impossible to determine at once whether the headache, delirium, muscular twitchings, retraction of the head, etc. are due to meningismus (see p. 90) or to true meningitis. Lumbar puncture is an indispensable aid to diagnosis. By this means it is usually possible not only to demonstrate the existence of a true meningitis, but to determine the exact nature of the infection. The distinctive features of meningococcic meningitis and tuberculous meningitis have already been considered (see pp. 55, 83).

**Prognosis.**—The outlook is always grave, and in the tuberculous form it is virtually hopeless. Pneumococcic meningitis is also usually fatal, but it may end in recovery. The duration is variable. Streptococcic and pneumococcic meningitis last, as a rule, from a few days to two weeks. The average duration of tuberculous meningitis is from 2 to 3 weeks Cerebrospinal fever usually runs an acute course of from 1 to 2 weeks, but it sometimes lasts a month or longer.

**Treatment.**—The general treatment coincides with that of cerebrospinal fever (see p. 90). Repeated lumbar puncture lessens the intracranial pressure and relieves the symptoms. Litchfield[1] has used a specific antipneumococcus serum intraspinally with good results in pneumococcic meningitis.

## SEROUS MENINGITIS OR MENINGISM

This term is used to designate a morbid process resembling true meningitis in its manifestations, but in which the cerebrospinal fluid is sterile and sometimes virtually normal in other respects. The condition is observed most frequently in the course of acute infectious diseases, such as pneumonia, typhoid fever, influenza, scarlet fever, mumps, septicemia, etc. It sometimes occurs as an accompaniment of the acute gastroenteritis of children. Oppenheim, Nolen, Pelz[2] and others speak of its occurrence in pregnancy or the puerperium. The cerebral symptoms do not differ materially from those of true meningitis although they are usually much less pronounced. The commonest manifestations are headache, delirium, hyperesthesia, exaggerated reflex activity, slight rigidity of the neck and twitching of the muscles. Vomiting or generalized convulsions may occur. The cranial nerves are rarely involved, but changes in the optic disc have been observed. The cerebrospinal fluid may be normal in amount, appearance and contents, but frequently it is under increased pressure, contains more cells (20 to 100 per cmm.) than is usually accepted as being normal, and shows an increased amount of globulin. Bacteriologically, it is negative. Not only may symptoms of meningismus develop without pronounced changes in the cerebrospinal fluid, but increased pressure and pleocytosis of the cerebrospinal fluid may occur in acute infectious diseases without symptoms of cerebral irritation. Probably in exceptional cases what is believed to be meningismus with normal or nearly normal cerebrospinal fluid is reality a true meningitis confined to a high level of the cerebrospinal system (meningitis circumscripta), the whole mass of subarachnoid fluid not being affected at the time by the inflammatory changes. Usually, but not invariably, the symptoms of meningismus are transitory and subside with improvement in the etiologic condition.

## CHRONIC CEREBRAL LEPTOMENINGITIS

Chronic cerebral leptomeningitis may be a continuation of the acute form; thus, some cases of cerebrospinal fever, particularly of the type occur-

[1] Jour. Amer. Med. Assoc., May 10, 1919.
[2] Berlin. klin. Woch., 1912, 1, No. 30.

ring in children below the age of two years (posterior basic meningitis), run a very chronic course. More frequently, the disease is chronic from the onset, and in this case it is usually the result of syphilis, tuberculosis, or alcoholism. Occasionally it accompanies or follows chronic pachymeningitis. The cortex almost always shares to some extent in the inflammatory process, making the condition really one of meningoencephalitis. The symptoms are variable. Among the most constant are dull persistent headache, somnolence, and impairment of the mental faculties. Focal symptoms of various kinds may also be present. Thus, when the lesion is over the motor area there may be convulsive attacks of Jacksonian type, and when the base is affected there may be evidences of pressure on one or more of the cranial nerves, such as inequality of the pupils, ptosis, strabismus, and optic neuritis. It is not always possible to distinguish between chronic leptomeningitis, especially when it is circumscribed, and *brain tumor*. The affection is a serious one and the prognosis must be guarded, even in syphilitic cases. If the process can be localized and is in an accessible region, trephining may be done and the induration removed.

## SPINAL PACHYMENINGITIS

Inflammation of the spinal dura mater is usually secondary to disease of the vertebræ, especially tuberculosis, but exceptionally it occurs as the result of traumatism or syphilis. The symptoms are mainly due to compression of the spinal cord and nerve roots by the exudation or to the direct invasion of these structures by the inflammatory process itself. Briefly, they consist of neuralgic pains, reflected along the irritated nerves to the thorax or abdomen, diminished flexibility of the back, tenderness of the spine, cutaneous hyperesthesia, and gradual loss of power in the legs, with increased reflexes and contracture of the muscles.

**Pachymeningitis Cervicalis Hypertrophica.**—This disease, first described by Charcot in 1871, is characterized by marked thickening of the dura mater in the cervical region, with consequent compression and degeneration of the nerve roots and superficial layers of the spinal cord. The etiology is obscure, although syphilis and traumatism seem to be factors of some importance. The first symptom to attract attention is neuralgic pain in the neck, shoulders and arms. This is usually severe and accompanied by tingling or formication in the arms and hands and more or less rigidity of the cervical spine. After the lapse of a few months the pain becomes less severe and a stage of paresis sets in, marked by increasing weakness and wasting in the muscles of the upper extremities, especially those supplied by the ulnar and median nerves. Eventually, the hands may assume the peculiar claw-like deformity seen in progressive muscular atrophy. The muscular tonus is usually, although not invariably, decreased. Areas of anesthesia are sometimes observed. At a still later period spastic paralysis of the lower limbs may develop as the result of a secondary degeneration of the pyramidal tracts of the spinal cord.

The disease may be distinguished from *amyotrophic lateral sclerosis* by the presence of conspicuous sensory symptoms and from *syringomyelia* by the absence of vasomotor disturbances, trophic alterations of the skin and joints, and the dissociation symptom (thermo-anesthesia and analgesia with preservation of tactile sensation). *Tumors of the cervical cord* produce in the initial stage the same symptoms as pachymeningitis but they pursue a more rapid course.

The prognosis of the disease should always be guarded, recovery or even decided improvement being of exceptional occurrence. Applications of

the Paquelin cautery to the back of the neck and the administration of potassium iodid are the therapeutic measures most likely to be of service.

## ACUTE AND CHRONIC SPINAL LEPTOMENINGITIS

*Acute inflammation of the spinal pia* is rarely seen except in association with acute inflammation of the cranial pia (acute cerebral leptomeningitis) or of the substance of the spinal cord (acute myelitis) and is referred to in the discussion of these diseases. *Chronic spinal leptomenigitis* usually occurs as an accompaniment of sclerosis of the spinal cord or as an extension of chronic pachymeningitis. It may be the initial lesion, however, in spinal syphilis. Pain in the back, radiating into the limbs, muscular rigidity, a girdle sensation, paresthesia, and finally paresis, partial anesthesia, and disturbances of the bladder and rectum are its most important symptoms.

## CIRCUMSCRIBED SPINAL SEROUS MENINGITIS

### (Circumscribed Cystic Spinal Meningitis)

This comparatively uncommon condition, first described anatomically by Schlesinger[1] in 1898, usually occurs as an accompaniment of lesions of the vertebræ, syphilitic or tuberculous meningitis, or chronic intramedullary disease, but it may occur as an independent affection, in some cases without obvious cause and in others as a result of traumatism or of a generalized infection.

The **symptoms** are those of tumor of the spinal cord, being first unilateral, as a rule, and later bilateral. Paresthesias of various kinds, hyperesthesia, actual pain and motor disturbances, usually paresis or paralysis, are almost always present. The reflexes are generally increased and there may be ankle-clonus and a Babinski's sign. The cerebrospinal fluid is usually clear and poor in cells, but of a yellow color and very rich in protein, sometimes undergoing spontaneous coagulation in the test-tube (syndrome of Froin). In the diagnosis, syphilitic meningomyelitis and traumatic lesions of the spine must be excluded. Differentiation from tumor is scarcely possible, but fortunately the necessity for it does not exist, as both conditions demand operative treatment.

## HEMORRHAGE INTO THE SPINAL MENINGES (HEMATORRHACHIS) AND INTO THE SPINAL CORD (HEMATOMYELIA)

Large hemorrhages into the membranes or into the substance of the cord arise chiefly from traumatism. In some cases they depend upon the erosion of a vessel caused by a spinal tumor or an aortic aneurysm. Occasionally intramedullary bleeding is the consequence of chronic arterial disease and occurs spontaneously or under violent effort, as in cerebral apoplexy. Scattered hemorrhages not infrequently occur in the course of meningitis or myelitis, the acute infectious diseases, convulsive disorders, such as tetanus, and in the various forms of purpura, but these are generally very small and without clinical significance.

**Symptoms.**—In both hematorrhachis and hematomyelia the symptoms usually appear abruptly. In the former severe pain is felt in the back and in the distribution of the nerves emanating from the spinal segments affected by the hemorrhage. The pain is increased by spinal movements and is nearly always accompanied by other indications of meningeal or root irrita-

[1] Beit. z. Kennt. d. Rückenm. und Wirbeltumoren, Jena, 1898.

tion, such as rigidity of the neck or back, hyperesthesia, paresthesia, involuntary muscular contractions and interference with micturition and defecation. Fluid obtained by lumbar puncture is bloody. In small extravasations there are no further developments and recovery, as a rule, is rapid and complete. In large hemorrhages medullary symptoms quickly follow. Briefly, these consist of a loss of motion and sensation in the parts supplied by the cord below the level of the lesion. Consciousness is rarely disturbed unless the bleeding effects the upper portions of the cord and is very copious. Death may occur within the first few days from shock or paralysis of the respiratory musculature. If the patient survives these dangers and no complications, such as cystitis or bedsores arise, the functions of the cord are likely to be completely restored with the absorption of the clot, but such a favorable termination is not to be assumed too confidently, as some degree of muscular atrophy or spastic paresis often remains.

*Hematomyelia* produces a clinical picture very similar to that of extensive meningeal hemorrhage and the distinction between the two conditions cannot always be made with certainty. Generally speaking, however, in intramedullary hemorrhage paralysis is present from the first and is pronounced and persistent, pain is circumscribed, signs of root irritation are slight or lacking, and the fluid removed by lumbar is clear. In the majority of cases, too, the symptoms are more marked on one side of the body than the other, and not rarely they take the form of Brown-Séquard's type of paralysis. In patients who recover from the first shock the affection pursues a course corresponding to that of transverse myelitis or, more rarely, to that of syringomyelia. Indeed, if myelitis begins abruptly, as is occasionally the case, there may be no way of distinguishing it from intramedullary hemorrhage. In any case, however, a spontaneous origin and an onset with fever are in favor of myelitis. Embolism of the abdominal aorta resembles hematomyelia in producing sudden paraplegia, but in this rare condition the femoral arteries do not pulsate and the legs are cold and livid.

# DISEASES OF THE PERIPHERAL NERVES

## NEURITIS

**Definition.**—Neuritis is an affection of the peripheral nerves, of an inflammatory or degenerative nature, characterized by sensory, motor, and trophic disturbances in the area of distribution. The process may be acute or chronic, and it may be confined to a single nerve or group of nerves (*localized neuritis*) or may involve many nerves at one time (*multiple neuritis*).

### LOCALIZED NEURITIS

**Etiology.**—The majority of cases of localized neuritis are of *traumatic* origin, the result of severing, contusion, compression or torsion of the nerve. Such injuries are common in fractures and luxations. To compression or stretching of the nerves must also be ascribed the cases of neuritis occurring in certain occupations, that follow immoderate use of the muscles or the prolonged maintenance of awkward positions, that develop in infants at birth in consequence of various obstetrics procedures, that occur in women during labor as a result of delay in the advancement of the presenting part or faulty

use of forceps, that develop in association with supernumerary cervical ribs, and, finally, most cases of post-anesthetic paralysis. Less frequently, localized neuritis results from gradual *compression of the nerve* by enlarged lymph-nodes, tumor, aneurysm, or callus, or from *direct extension of an inflammatory process from contiguous tissues*. In the case of superficially situated nerves, such as the facial, it must be conceded that *exposure to cold* may act as an exciting cause. Pronounced *ischemia*, if persistent, is likely to result in neuritis. The degenerative neuritis occurring in obliterative endarteritis, in some cases of Raynaud's disease, and occasionally in arteriosclerosis is apparently due to interference with the blood-supply of the part. The neuritis developing in the course of infectious diseases (diphtheria, syphilis, typhoid fever, etc.) and chronic intoxications (lead, sulphonal, etc.), although usually more or less disseminated, may be confined to a single nerve or nerve-group. Undoubtedly general infections and intoxications make the nerves more prone to degenerative changes upon slight injury, even moderate compression.

**Morbid Anatomy**—Neuritis resulting from traumatism or extension of inflammation from contiguous tissues is usually of the *interstitial* variety. It may be associated with changes in the nerve-fibers but, as a rule, these are secondary to the inflammatory process. On the other hand, neuritis of toxic origin is essentially *parenchymatous*, any inflammatory changes occurring in it being secondary to a primary degeneration of the fibers. In acute interstitial neuritis the nerve is red and slightly swollen. Microscopic examination reveals dilatation of the blood-vessels and pronounced round-cell infiltration. More or less degeneration of the myelin and axis-cylinder is also commonly observed. In chronic cases the nerve is firmer and paler than normal and exhibits microscopically a great increase of fibrous tissue.

In parenchymatous neuritis the changes are similar to those occurring after section of a nerve (Wallerian degeneration), namely, disintegration of the myelin, proliferation of the nuclei of the sheath of Schwann, and swelling, fragmentation and finally complete destruction of the axis-cylinder. If the cause ceases to operate before any serious damage has been done, regeneration of the fibers may ensue, otherwise the parenchyma of the nerve entirely disappears and is replaced by fibrous tissue. In many cases of neuritis the cell-bodies in the anterior horns of the spinal cord, in the spinal ganglia or in the corresponding cerebral ganglia share to a greater or less extent in the degenerative process, and, further, the muscles supplied by the affected nerves present various degrees of secondary atrophy.

**Symptoms.**—Pain in the area of distribution of the affected nerve is usually a conspicuous symptom. It is often severe and is intensified by movement. Pressure also increases it. In addition to pain there are various disturbances of sensibility, at first paresthesia and hyperesthesia, and later hypesthesia, or exceptionally complete anesthesia. Even when tactile sensation is much reduced slight irritation may cause pain (*anesthesia dolorosa*).

In the majority of cases impairment of muscular power, ranging according to the severity and extent of the disease, from slight weakness to actual palsy, accompanies the sensory disturbances. Owing to the manifold anastomoses of the sensory fibrils in the skin, sensation is ordinarily restored well in advance of the motor function. The paralyzed muscles become flaccid and, unless the conducting functions of the nerve-fibers are soon restored, undergo atrophy. The tendon-reflexes are almost invariably decreased or abolished. Ultimately, in severe cases, various deformities, such as *claw hand* in ulnar neuritis and *equinovarus* in peroneal neuritis, ensue, first from contraction

of the healthy unopposed muscles and later from atrophic shortening of the degenerated ones.

The electric reactions are soon changed. In the milder forms of the disease there may be merely a diminution of excitability, but in severe cases with marked atrophy, a partial or total reaction of degeneration is often found. Trophic and secretory disturbances in the parts supplied by the affected nerves are not uncommon. The skin may take on a peculiar smooth, glistening, rosy appearance (*glossy skin*); the nails may become rough, furrowed and brittle; the hair may grow excessively or fall out; bullous or herpetic eruptions may develop, or profuse sweating may show itself.

**Course.**—The course varies with the intensity of the disease. In the majority of cases the symptoms gradually disappear after the removal of the cause and the institution of appropriate treatment. Months or even years, however, may elapse before the function of the part is fully restored.

**Diagnosis.**—The diagnosis of neuritis is seldom difficult. Especially significant are the limitations of the sensory disturbances to an area corresponding to the anatomical distribution of the nerve and the occurrence of tenderness along the nerve-trunk itself. In ordinary *neuralgia* the pain is paroxysmal, the tenderness is limited to definite points, and there is no loss of sensibility or of muscular power.

**Treatment.**—Removal of the cause, if possible, and absolute rest of the affected part are the first requisites of treatment. When the nerves of the limbs are involved it may be necessary to use splints and bandages to prevent muscular action. Moist heat in the form of compresses or of local hot baths is often beneficial. Occasionally, cold applications are more effective. A saturated solution of magnesium sulphate on several thicknesses of gauze may be used. In less acute cases counter-irritation by means of small blisters or the Paquelin cautery at points where the nerve-trunk is especially tender sometimes affords relief. In mild forms of the disease ointments of belladonna and methyl-salicylate may suffice. When the pain is very persistent exposure of the part to superheated air in a Tallermann apparatus may have a good effect. Of the analgesics, the coal-tar derivatives, acetphenetidin and the salicylates, are, as a rule, the most useful. A combination of these drugs with codein is especially efficacious.

℞ Acetphenetidini..... ℥i (4.0 gm.)
Acidi acetylsalicylici..... ℥iss (6.0 gm.)
Codeinæ sulphatis..... gr. iii (0.2 gm.) M.
Ft. chart. No. xii.
Sig.—One every three or four hours.

Morphin should be used only as a last resort. After the symptoms of irritation have completely subsided the indications are to maintain nutrition in the paralyzed muscles by systematic massage and electrical treatment and to prevent contracture in the muscles and stiffness of the joints by passive movements. When faradic contractility is lost, which is frequently the case, labile or interrupted galvanic currents should be employed, with that pole applied to the muscles which gives the better contractions. In traumatic cases, which show no tendency to recover after several months, surgical intervention (removal of cicatricial tissue with suture of the divided nerves, nerve anastomosis, or tendon transplantation) should be considered.

## MULTIPLE NEURITIS

**Etiology.**—Multiple neuritis frequently results from the action of certain *exogenous poisons*, such as alcohol, lead, arsenic, mercury, carbon dioxid, and

coal-tar derivatives, particularly sulphonal and trional. Of these alcohol is the most important. Many cases develop during or after *infectious diseases*. Diphtheria, typhoid fever, influenza, and septicemia are especially potent in this respect, but probably no infection can be omitted from the list. Occasionally, rheumatism, syphilis, tuberculosis, gonorrhea, malaria or tetanus is a factor. During the World War an acute, specific infectious disease, characterized by fever, headache, and polyneuritis was observed among the British troops. The infection, which seemed to be allied to acute poliomyelitis on the one hand and to epidemic encephalitis on the other, could be reproduced in monkeys. Of 30 cases reported by Bradford, Bashford and Wilson[1] death occurred in 8. A special type of multiple neuritis is a feature of *leprosy*. Lerporsky[2] has described a number of cases in which no cause was apparent other than *tapeworm infestation* (Dibothriocephalus latus) and which promptly subsided after expulsion of the parasite.

Multiple neuritis not infrequently occurs in the course of diabetes, pernicious anemia and other cachectic conditions, doubtless in consequence of the development of certain *autocthonous* poisons which act destructively upon the nerves. To endogenous intoxication must also be ascribed neuritis that is occasionally observed in gout, in pregnancy, and after sunstroke. The cases that have been described as *idiopathic* because of their cryptogenic origin, probably belong to the toxic group, but whether the inciting agent is endogenous or exogenous is a question that future study must solve. Barker and Estes[3] have ascribed a rare syndrome, consisting of digestive disturbances, hematoporphyrinuria, epileptiform seizures and polyneuritis, to a toxemia resulting from gastroduodenal dilatation. The multiple neuritis occurring in beriberi (see p. 348), a disease endemic in China, Japan, and various tropical countries, is apparently an effect of *malnutrition* caused by the absence of certain essential constituents in the diet. A distressing and intractable form of neuritis is occasionally seen in the aged, probably as a result of *arteriosclerosis* and disturbances in general nutrition. Finally, neuritis may occur as *a part of organic disease of the central nervous system*, notably in cerebrospinal syphilis, tabes dorsalis and taboparesis.

**Morbid Anatomy.**—In multiple neuritis the nerve-fibers themselves are mainly involved in a process of degeneration and atrophy (parenchymatous neuritis), the connective-tissue elements being only secondarily affected. Changes in the cells of the central nervous system are present in many cases.

**Symptoms.**—In its most severe form multiple neuritis begins suddenly with chilliness and pronounced febrile disturbance (101°–103° F.), followed by headache, backache and prostration. The neural localization of the process is soon made apparent by paroxysmal pain, paresthesia, general muscular soreness, and tenderness of the nerve-trunks to pressure. Complete anesthesia is rarely observed, but some degree of hypesthesia is almost always present. Paresis also appears early. It may develop simultaneously in all four limbs, but more frequently it begins in the legs and then extends to the arms. In malignant cases the muscles of the trunk and the diaphragm soon become involved and death occurs in a few day from asphyxia. As a rule, the paresis is more or less symmetrical, affects the legs to a greater extent than the arms, and is more pronounced in the distal than in proximal portions of the limb. Among the cranial nerves, the vagi and those supplying the external ocular muscles are most often affected. Disturbance of the sphincters is exceptional, and when it does occur, is probably indicative

[1] Quar. Jour. Med., Jan., 1919.
[2] Russky Vratch, 1915, xiv, No. 38.
[3] Jour. Amer. Med. Assoc., Aug. 31, 1912.

of concomitant changes in the spinal cord. The paretic muscles become soft, rapidly waste and soon yield a partial, or rarely a complete, reaction of degeneration. Edema sometimes obscures the atrophy. The tendon reflexes are abolished or are much decreased.

In *chronic multiple neuritis* there is slowly increasing loss of power, beginning, as a rule, in the legs and later involving the arms. The extensors of the feet and hands especially suffer, and hence foot-drop and wrist-drop are characteristic features. If the patient is able to walk his gait is also peculiar. To avoid dragging his pendent toes he raises the foot and knee abnormally high, throws the foot forward and then brings it down to the floor without undue force, the whole movement giving the appearance of one stepping over high obstacles (*steppage gait*). Rarely the paresis appears earlier and is more pronounced in the arms than in the legs, and possibly in very exceptional cases it may be unilateral. In some instances the cranial motor nerves become involved, those of the eye and face being most liable to invasion. In grave cases the vagus may be implicated, as revealed by undue frequency and irregularity of the pulse. Optic neuritis has been observed in a few instances. Bladder disturbances are exceptional, and when they do occur are usually transitory. The paresis being of a degenerative type, is accompanied by atrophy of the muscles, changes in electric contractility and abolition of the tendon reflexes. For a long time the affected muscles remain soft and flaccid, but ultimately they become indurated from cirrhotic changes, and then contractures appear.

Sensory disturbances, consisting of spontaneous pain, various forms of paresthesia, hyperesthesia, tenderness over the nerve-trunks, hypesthesia, and hypalgesia, are prominent in the majority of cases, and occasionally dominate the clinical picture (*sensory type of multiple neuritis*). In some instances, owing to impairment of deep sensation, ataxia is also present. When this feature is conspicuous and the paretic symptoms are poorly developed the disease bears a close resemblance to locomotor ataxia. To such cases the names neurotabes peripherica (Déjérine) and ataxic polyneuritis (Remak) have been given. On the other hand, in a small number of cases the only sensory disturbance is slight paresthesia, and even this may disappear before the disease is far advanced (motor type of multiple neuritis).

Vasomotor and trophic phenomena are much less constant than motor and sensory disturbances, but edema of the feet and hands, hyperidrosis, glossy skin, and deformity of the nails are not uncommon. Occasionally, painful swelling of the joints is met with, simulating articular rheumatism, but what relation this condition holds to the neuritis is not clear.

In severe cases mental symptoms often precede or follow the physical signs. They are most common in alcoholic neuritis, but are not infrequent in other forms of the disease. Especially characteristic is the syndrome first fully described by Korsakow,[1] the cardinal features of which are defective memory, particularly for recent events, loss of orientation, spurious reminiscence, pronounced fabrication, easily provoked mental confusion, and in some cases definite hallucinations of sight and hearing. These symptoms may arise out of a depressive or stuporous state, out of a ordinary hallucinatory delirium or, in alcoholic cases, out of ordinary delirium tremens. Permanent mental impairment, more or less pronounced, is common after Korsakow's psychosis, but complete recovery is not impossible.

**Course.**—The course of the disease varies with the severity and extent of the lesions. In acute cases death may result in a few days from paralysis of the respiratory muscles, heart failure, or complicating pneumonia. The

[1] Arch. f. Psych., 1892, Bd. xxi, 669.

occurrence of marked mental symptoms makes the outlook more grave. In chronic cases, if the cause can be removed and the patient's health has not already been seriously undermined by excesses or other diseases, the outlook is generally good, both as to life and the ultimate restoration of power. Months and years, however, sometimes elapse before recovery is complete, especially when there is much wasting of the muscles. In some cases recovery is only partial, a certain amount of weakness and deformity remaining permanently in the distal ends of the extremities.

An attack of neuritis, even when it ends in complete recovery, seems to increase the vulnerability of the nerves, and therefore it is not exceptional to observe two or more recurrences in the same individual (*polyneuritis recurrens*).

**Diagnosis.**—The diagnosis is not usually difficult. The significant features are the history or the evidence of antecedent infection, intoxication or cachexia, the more or less symmetrical distribution of the motor and sensory disturbances and their greater development in the distal ends of the limbs, the predominance of the paresis in the extensor muscles, the tenderness of the nerve-trunks, the diminution or abolition of the tendon reflexes and the maintenance of sphincteric control.

*Tabes dorsalis* may be excluded by the peculiar distribution (segmental) of the hypesthetic areas, especially on the trunk, by the occurrence of the girdle sensation, lightning pains, crises, Argyll-Robertson pupil, and sphincteric disturbances, by the early loss of muscular sense, by the characteristic changes in the cerebrospinal fluid, and by the absence of tenderness over the nerve-trunks and of muscular atrophy.

In *acute myelitis* there is no tenderness of the nerves or muscles, the palsy shows no predilection for the extensor muscles or for the distal ends of the extremities; the loss of sensation is more complete and more uniformly distributed over the limbs and trunk; the sphincters are always involved; cystitis is a common complication; and bed sores appear early. In *Landry's disease* sensory disturbances are rarely conspicuous, the nerve-trunks are not tender, trophic changes are usually absent, and the paralysis shows a marked tendency to ascend and invade the nerves innervated from the medulla.

In *acute poliomyelitis* pain may be absent, and if present is usually transitory; paresthesia is never conspicuous; the nerve-trunks are not especially tender; and the palsy develops abruptly, is often asymmetrical, is more pronounced in the proximal portions of the limbs, and always recedes to some extent upon improvement in the patient's general condition, the muscles of distal parts recovering first.

*Spinal progressive muscular atrophy* may be recognized by its extremely slow onset, by its predilection for the muscles of the hands and shoulders, by the occurrence of fibrillary twitchings, and by the almost complete absence of sensory disturbances.

**Treatment.**—Careful search should be made for the exciting cause with the view of removing it, if possible. In all cases, except mild forms involving only the arms, rest in bed is essential, and if the pain is severe a water-bed is desirable. To avoid shortening of the calf muscles, the legs, so far as possible, should be kept extended, and to prevent foot-drop, the pressure of the bed-clothes should be removed by wire hoops and the soles supported by pillows or sandbags. The diet must be abundant and nutritious, but easily digestible. The pain is often relieved by warm fomentations or gentle friction with warm oil. Occasionally, however, cold applications afford more comfort. Such drugs as acetphenetidin and the salicylates are usually

required, but they must not be used continuously on account of their depressant effects. In some cases the pain is so intense that morphin must be employed.

In the chronic stage warm baths, massage, electricity, passive movements, and educational gymnastics are the measures to be employed in promoting the nutrition of the affected muscles and aiding in the repair of the damaged nerves. Tonics, especially strychnin and iron, are also of value. Convalescence is often hastened by a change of air and scene. In long-standing cases with contractures and deformities surgical intervention may be necessary.

## SPECIAL FORMS OF NEURITIS

**Alcoholic Neuritis.**—This is the most common form of multiple neuritis. It results chiefly from overindulgence in spirituous liquors, although beer and ale are not without influence. Tipplers are much more likely to become victims than those who only occasionally drink to excess. Although numerically more males are attacked than females, the disease is relatively more frequent in women than in men.

The course of alcoholic neuritis may be chronic throughout, or there may be an acute onset preceded by a prodromal period marked by digestive disturbances, insomnia, generalized neuralgic pains and muscular cramps. The subjective sensory disturbances are usually very conspicuous; foot-drop and wrist-drop appear early and are well developed; ocular symptoms, especially amblyopia, inequality of the pupils and moderate myosis, are not uncommon; incoördination is sometimes so marked as to suggest locomotor ataxia; psychic phenomena, in the form of mental confusion, hallucinatory delirium, or the almost characteristic Korsakow's syndrome, are seldom absent in severe cases. In rare instances palsy of the ocular muscles and optic neuritis are associated with the ataxia of gait and mental disturbance, thus producing a clinical picture of the disease first described by Wernicke as *polioencephalitis superior.*

**Plumbic Multiple Neuritis.**—In the majority of cases lead palsy does not extend beyond the muscles of the forearm and hands; it affects chiefly the extensors, producing the suggestive wrist-drop, and spares the long supinator and, for a considerable period, the long abductor of the thumb; and it is not attended by sensory disturbances, except, perhaps, slight paresthesia over the backs of the hands and forearms. Atrophy of the Aran-Duchenne type, involving the small muscles of the hands, or of the Erb type, involving the muscles of the shoulders and upper arms, is occasionally seen. The lower extremities are rarely affected, at least in adults. A few cases of acute generalized saturnine palsy, however, have been described. Other indications of lead poisoning, such as the blue line on gums, obstinate constipation, colic, basophilic granulation of the erythrocytes, are almost always present to aid in the diagnosis.

**Arsenical Multiple Neuritis.**—Neuritis may be a manifestation of either acute or chronic arsenical poisoning. The motor and sensory symptoms resemble those of the alcoholic form. The paralysis, while showing a predilection for the legs, frequently involves all four extremities; sensory disturbances are usually prominent; and ataxia is common and sometimes precedes the paralysis. The most distinctive feature, however, is the marked tendency to vasomotor and trophic disturbances, as manifested by hyperidrosis, abnormal pigmentation of the skin, herpes, erythematous rashes, and excessive epidermic accumulations (keratosis) on the palms and soles.

**Neuritis of Pregnancy.**—Under this heading may be included those rare cases of neuritis that develop during pregnancy or early in the puerperium

and which are not traceable to any of the well-recognized causes of neuritis, but are probably due to the action of some endogenous poison. Indeed, the condition is usually preceded by pernicious vomiting and pronounced acceleration of the pulse. True gestatory neuritis is not to be confused with (1) that occurring in pregnant women as a result of alcoholism or other exogenous poisoning; (2) that occurring during labor as a consequence of compression of the pelvic nerves by the fetal head or forceps (peroneal type); or (3) that developing during the puerperium as a result of local or general sepsis. In the neuritis of pregnancy the inflammation may be limited to one or two nerves or it may be general. Not rarely the symptom-complex resembles that of acute myelitis or Landry's disease. Indeed, in some of the fatal cases changes have been found in the spinal cord as well as in the peripheral nerves. Psychic disturbances are not uncommon. Twenty per cent. of 46 severe cases compiled by Hoesslin[1] terminated fatally.

## DISEASES OF INDIVIDUAL PERIPHERAL NERVES

### THE FIRST OR OLFACTORY NERVE

Disturbances of smell may result from lesions affecting any portion of the olfactory nerves or tracts from the peripheral terminations in the Schneiderian membrane of the nose to the centers in the brain (hippocampal cortex).

**Anosmia,** or loss of smell, may be caused (1) by various lesions in the nasal cavities, such as acute and chronic rhinitis, polypi, caries of the ethmoid bone, abnormal dryness of the mucous membrane from palsy of the fifth nerve; (2) by lesions of the nerves at the base of the brain, such as may result from meningitis, tumors in the anterior fossa, fracture of the cranial bones; (3) by atrophy of olfactory nerves, such as seems to occur occasionally in senility and tabes dorsalis; (4) by hysteria; (5) rarely by lack of development or disease of the olfactory centers.

In testing the sense of smell, substance that will not simultaneously irritate the fifth nerve should be avoided. Asafetida and musk are suitable for the purpose. Impairment of the sense of taste usually accompanies anosmia of organic origin.

**Subjective sensations of smell (parosmia)** are occasionally observed as hallucinations in insanity and as auræ in epilepsy. In a few instances perversions of smell have been produced by tumor in the central olfactory area.

**Hyperosmia,** or increased sensitiveness of the sense of smell, is occasionally observed in hysteria and other neuroses.

### THE SECOND OR OPTIC NERVE

**Retinitis.**—Inflammation of the retina is of interest to the practitioner of internal medicine because it is often a local manifestation of general disease. Especially important is the retinitis occurring in nephritis, syphilis, leukemia, diabetes, arterial disease, and severe forms of anemia. Ophthalmoscopic examination reveals diffuse or circumscribed cloudiness of the retina, areas of exudation, tortuosity of the vessels, hemorrhagic extravasations, redness of the nerve-head, and often spots of atrophy from antecedent hemorrhages or areas of inflammation. These changes are accompanied by

[1] Münch. Med. Woch., 1905, No. 14.

impairment and distortion of vision, and sometimes by dull pain and photophobia. It is noteworthy, however, that vision may be fairly good even when the objective indications are pronounced. Exudation in the form of a white star-shaped figure in the region of the macula or of broad white ring around the nerve-head ("snowbank" appearance) is strongly suggestive of albuminuric retinitis. As a rule, both eyes are affected.

**Optic Neuritis.**—Two forms of inflammation of the optic nerve are recognized: One in which the intra-ocular end of the nerve is the seat of definite lesions, and another in which this portion of the nerve presents a normal or nearly normal appearance. The first form, the more important of the two from a neurologic viewpoint, is known as *intra-ocular optic neuritis* or *papillitis*, the second, as *retrobulbar* or *orbital optic neuritis*.

*Papillitis* is most frequently caused by tumor of the brain, especially of the basal ganglia, parieto-occipital region, and cerebellum, but is not uncommon in intracranial syphilis, abscess of the brain, cerebral hemorrhage, internal hydrocephalus, meningitis and thrombosis of the cavernous sinus. Less frequently it is observed as a result of focal infection in the paranasal sinuses, middle ear, teeth or tonsils; of periostitis in the orbital region; of a general infection, such as influenza, scarlet fever, smallpox, etc.; of poisoning by various agents, including lead, alcohol, organic arsenic compounds, male-fern; or of chronic nephritis. Occasionally it accompanies severe anemia, general paresis, disseminated sclerosis, or myelitis.

The ophthalmoscopic features of papillitis are as follows: The disc is swollen and congested; its margins are obscured; the arteries are constricted; the veins are dilated and tortuous; hemorrhages are often present. Swelling of the papilla of a distinctly measurable height is generally referred to as *choked disc*. The prominence may be 2 or 3 mm. or more. Such high grades of papilledema are particularly significant of increased intracranial pressure. In many cases vision remains unaffected for a long period.

The exact manner in which choked disc is brought about is not definitely known. According to one view (von Leber) it is primarily a toxic neuroretinitis set up by some irritant that reaches the disc by way of the vaginal sheath. According to another view (Manz and Schmidt-Rimpler) it is primarily a neuroretinal edema (with cellular infiltration and atrophy of the disc as secondary features), produced mechanically by a venous engorgement and a backing up of subarachnoid fluid in the optic sheath. The last theory has received strong support from the results of the experiments of Bordley and Cushing[1] and of Parker[2] and from the observations of von Bruns, Paton, Frazier and others on the retrocession of choked disc after decompressive cranial operations.

*Retrobulbar optic neuritis* may be due to some general infection, to focal infection in the paranasal sinuses, tonsils, teeth, etc., to orbital periostitis, or to poisoning by certain agents, such as alcohol, tobacco, atoxyl, nitrobenzol, etc. Retrobulbar neuritis on the side of the lesion and choked disc in the opposite eye are suggestive of tumor or abscess of the frontal lobes (Kennedy). The chief symptom of the condition is diminution of sight, beginning in the center of the visual field. The ophthalmoscopic appearances may be negative, but in chronic cases there may be pallor, especially on the temporal half the papilla, and in the later stages of acute cases there may be slight congestion of the disc with obscuration of its margins and contraction of the retinal arteries.

**Atrophy of the Optic Nerve.**—Three forms are recognized: (1) *Primary*

[1] Jour. Amer. Med. Assoc., Jan., 1909.
[2] Jour. Amer. Med. Assoc., Oct. 7, 1916.

*atrophy*, which is of frequent occurrence in tabes dorsalis, paretic dementia, and multiple sclerosis, and which is sometimes seen in amyotrophic lateral sclerosis, in diabetes, in syphilis, in arteriosclerosis, in poisoning by certain drugs, and in excessive hemorrhage; (2) *secondary atrophy*, which results from pressure upon the optic tract by tumors, cysts, hydrocephalus, etc.; (3) *consecutive atrophy*, which follows inflammation of the optic nerve, choroid or retina. Ophthalmoscopic examination discloses an alteration in the color of the disc varying from slight gray to clear white, depression of the disc, broadening of the scleral ring and contraction of the vessels.

The pupils are usually dilated and unresponsive to light. Subjectively, there are reduced acuteness of central vision, sometimes amounting to complete blindness, and contraction of the field to vision for white and for colors.

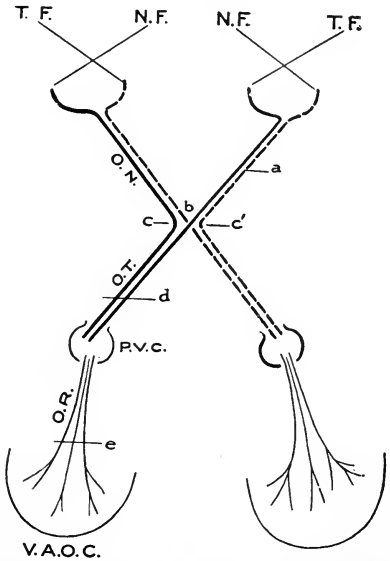


FIG. 32.—Diagram of optic system. T..F, temporal field; N.F., nasal field; ON., optic nerve; O.T., optic tract; P.V.C., primary visual centers (ext. geniculate body, pulvinar of thalamus and sup. quadrigeminum); V.A.O.C., visual area in occipital cortex. A lesion at a produces unilateral nasal hemianopsia; at b, bitemporal hemianopsia; at c, unilateral nasal hemianopsia; at c and c', binasal hemianopsia; at d or e, homonymous hemianopsial.

*Hereditary Optic Atrophy.*—Retrobulbar neuritis ending in optic atrophy is occasionally observed as an hereditary and familial disease, which develops, as a rule, during adolescence. Only about 12 per cent. of 300 recorded cases have been in women (Guzmann[1]). The disease is transmitted chiefly by unaffected females. Recovery is rare.

**Disturbances of Vision Without Changes in the Fundus.**—In certain conditions impairment of vision (amblyopia) or even complete blindness

[1] Wien. klin. Woch., 1913, xxvi, No. 4.

(amaurosis) may occur without ophthalmoscopic changes. These conditions include hysteria, uremia, and poisoning by certain substances, such as lead, tobacco and alcohol. Toxic amblyopia is due in many instances to retrobulbar neuritis.

**Hemianopsia.**—This is a loss of one-half of the visual field. It may result from a lesion involving the optic chiasm or the optic tract at any point between the chiasm and the visual area in the occipital lobe. As a transitory condition it is sometimes observed in migraine. Hemianopsia is *horizontal* or *vertical* according as the line separating the lost from the preserved field is horizontal or vertical. *Horizontal* hemianopsia may be due to a lesion exerting downward pressure on one optic tract or pressure upon the upper or lower part of the chiasm, or upon the upper or lower part of the optic nerves.

*Vertical Hemianopsia.*—Blindness involving the two right halves or the two left halves of the visual fields is referred to as *homonymous hemianopsia*, and blindness involving the two nasal halves or two temporal halves of the fields is known as *heteronymous hemianopsia.*

*Homonymous lateral hemianopsia*, the most common form of hemianopsia, may be produced by a lesion in the occipital lobe, the optic radiations, the internal capsule, the primary optic centers, or the optic tract. It has rarely been observed in migraine. *Bitemporal hemianopsia* can only result from a lesion involving the middle of the chiasm and destroying the conductivity of the crossed, but not the non-crossed, fasciculi. It is frequently observed in disease of the pituitary body. *Binasal hemianopsia* is rare and can arise only from symmetrical lesions affecting the outer portions of the chiasm or outer portion of each optic nerve.

## THE THIRD, FOURTH AND SIXTH CRANIAL NERVES

Lesions producing paralysis of the ocular muscles may be in the orbit, at the base of the brain, at the nuclei, or in the cortex. In many instances the nerve-trunks are injured by a morbid process at the base of the brain, such as gumma, tumor, meningitis, thrombosis of the cavernous sinus, and aneurysm of the basilar artery. Fractures involving the base of the skull or orbit are frequently accompanied by paralysis of the ocular muscles. In other cases inflammatory conditions or tumor of the orbit or diseases of the nasal accessory sinuses play an etiologic rôle. Tabes dorsalis, paretic dementia, and disseminated sclerosis frequently cause ocular palsies. Loss of power in the muscular apparatus of the eyeball is a conspicuous feature in superior polioencephalitis. Even in acute poliomyelitis the ocular muscles are sometimes affected. Paralysis of the external rectus or more rarely of other muscles of the eye sometimes follows spinal anesthesia. The external rectus is occasionally affected also in the course of otitis media. Hemorrhages, tumors and other focal lesions of the cerebral cortex or corticopeduncular region frequently involve the motor nerves of the eye.

In another large group of cases ocular palsies depend upon some infection or intoxication. Among the infections, syphilis, epidemic encephalitis, diphtheria, influenza and herpes zoster of the cephalic extremity are most important and among the toxic processes botulismus and lead poisoning deserve special mention. In these cases the lesion may be nuclear or peripheral. In rare instances oculomotor paralysis occurs periodically in association with migraine (ophthalmoplegic migraine). Congenital paralysis of one or more of the external ocular muscles is not uncommon and occasionally palsies occur without a recognizable cause.

Paralysis of one or more of the ocular muscles is manifested by strabismus

or, if slight, by immobility of the eye when attempts are made (with the head fixed) to rotate it in the direction of vision normally accomplished by the muscle affected. Efforts at rotation in that direction are sometimes productive of nystagmus. In consequence of the asymmetry in the movements of the two eyes double vision (diplopia) is a common symptom, especially at the beginning of the paralysis. Vertigo may also be present. It differs from other forms of dizziness in that it disappears upon closing the eyes.

Paralysis of the **third,** or **oculomotor nerve,** if *total*, causes ptosis, or drooping of the upper lid, deviation of the eyeball outward and downward, moderate mydriasis, and a complete loss of pupillary reaction both to light and accommodation. In *partial* paralysis the symptoms vary according to the branch of the nerve affected; thus, there may be isolated ptosis (levator palpebræ), divergent strabismus (internal rectus); deviation of the eyeball upward and outward (inferior rectus), or deviation of the eyeball downward and inward (inferior oblique).

**Recurrent Oculomotor Paralysis.**—This rare condition, termed by Charcot[1] *migraine ophthalmoplegique* usually develops in youth. It is characterized by recurrent attacks of migraine-like headache, vomiting and unilateral oculomotor paralysis. The paralysis, which may be partial or total, may entirely disappear in the intervals, or it may persist to some extent and increase with each succeeding attack. The latter type has usually been associated with some organic basal lesion, such as tumor or meningitis. It must not be forgotten that recurrent oculomotor palsy is sometimes the first symptom of a general disease of the nervous system, such as tabes or disseminated sclerosis, and that recurring diplopia is occasionally a forerunner of myasthenia gravis.

Isolated paralysis of the **fourth,** or **trochlear nerve,** which supplies the superior oblique muscle is rare. It is occasionally found with basilar meningitis and lesions involving the anterior portion of the cerebellum. In a few instances has been associated with migraine. More frequently the third and fourth nerves are involved together. In trochlear paralysis the direction of the affected eye is upward and inward and the disability is especially noticeable when the test-object is moved downward and inward. More characteristic, however, is vertical homonymous diplopia, the image of the affected eye being lower than its fellow and inclined to the sound side, and the diplopia becoming maximal when the patient looks downward and to the left.

Paralysis of the **sixth nerve** (*abducens*) may arise from the same causes that produce oculomotor palsy. Owing to the long course of the nerve unilateral or bilateral paralysis is comparatively frequent in tabes dorsalis. As Gradenigo[2] pointed out, it occasionally occurs in the course of purulent otitis media, as a result of simple serous or suppurative leptomeningitis. It has not rarely followed spinal anesthesia. In a few instances it has been observed in association with migraine. In abducens paralysis (external rectus) there is convergent strabismus and lateral homonymous diplopia.

**Ophthalmoplegia.**—This termed is used to designate paralysis of all the muscles of the eye or of the muscles innervated by two nerves, one of which is the third nerve. It is said to be *total* if all the muscles, both internal and external, are involved, and *partial*, if only one of these two groups are affected. Total ophthalmoplegia is characterized by drooping of the upper lid, immobility of the globe and unresponsiveness of the pupil to light, accommodation or convergence. Partial ophthalmoplegia is *internal* when it affects only the sphincter of the iris and the ciliary muscle, and *external*

[1] Progress Méd., 1890, xii, 31.
[2] Archiv. f. Ohrenheilkunde, 1907, vol. lxxiv.

when it involves only the upper lid and the extrinsic muscles of the globe.

Ophthalmoplegia may depend upon lesions involving the nuclei of the nerves of the eye muscles or the roots of the nerves as they pass through the cerebral axis. It may be due to hemorrhage, embolism, syphilis, areas of sclerosis, tumor, etc. It may occur in epidemic encephalitis, in botulism, in poisoning by certain agents, such as lead, nicotin, and carbon monoxid, and very rarely in migraine (Brissaud, Hunt). It is occasionally hereditary. Bradburne[1] observed it in 5 generations. Two special forms of nuclear ophthalmoplegia are recognized. The acute form, which was described by Wernicke under the name acute superior polioencephalitis, is of infectious or toxic origin and closely related to acute poliomyelitis; indeed, nuclear ophthalmoplegia occasionally occurs in epidemic poliomyelitis. The chronic form is a slowly progressive affection of a degenerative nature, analogous to chronic poliomyelitis.

Internal ophthalmoplegia is rare. It is presumably the result of a nuclear lesion and is usually due to syphilis.

**The Argyll-Robertson Pupil.**—In certain conditions the pupil reacts to accommodation and to convergence, but is insensitive to light. This phenomenon is known as the Argyll-Robertson pupil. It is nearly always bilateral and for some unknown cause it is, as a rule, accompanied by myosis. In testing for the reaction it is important to examine each eye separately and to bear in mind that in the aged and in the alcoholic the pupillary response to light is often weak, even when no organic disease exists. The site of the lesion is not definitely known. It is probably in the centripetal fibers of the pupillary light reflex at point between their separation from the visual fibers and the oculomotor nucleus. The Argyll-Robertson pupil is almost invariably a sign of tabes dorsalis, paretic dementia or cerebrospinal syphilis. It was associated with one of these three conditions in 94.7 per cent. of 1639 cases analyzed by Bach.[2] Occasionally, it is seen in other cerebral diseases and in alcoholic polyneuritis.

**Spasm of the Ocular Muscles.**—The orbicularis palpebrarum (blepharospasm) is the muscle usually affected. The contractions may be clonic or tonic. Clonic blepharospasm usually depends upon errors of refraction or or inflammation of the conjunctiva or eyelids. In some cases it takes the form of a tic. Tonic spasm of the orbicularis is usually a result of irritation of the peripheral filaments of the trigeminal nerves or to hysteria. According to de Schweinitz it was common in so-called shell-shock. Hysterical contraction of the orbicularis may simulate paralytic ptosis.

Spasm of the internal recti (spastic strabismus) is occasionally seen in hysteria. It may be mistaken for paralysis of the abducens.

**Nystagmus.**—This consists in involuntary, rapid oscillations of the eyeballs, due to clonic contractions of the ocular muscles. The movements may be lateral, rotary, or, rarely, vertical, and may be constant or present only when the eyes are moved in certain directions. Nystagmus occurs in many diverse conditions. It may be hereditary and familial; it may be congenital occurring with various defects of the eyeballs; it is common in albinism; it is often associated with acquired affections of the eye that impair vision; it sometimes depends upon chronic fatigue of the ocular muscles; it occurs in labyrinthine disease and in this type the movements are of unequal rapidity and are intensified when the eyes are turned in the direction of the rapid movement; it is not uncommon in miners who work in cramped positions (muscle fatigue); and it is observed in certain organic

[1] Brit Med. Jour., Feb. 3, 1912.
[2] Bach, Pupillenlehre, 1908.

diseases of the brain, especially in disseminated sclerosis, Friedreich's ataxia and tumors of the cerebellum.

## THE FIFTH OR TRIGEMINAL NERVE

The sensory and motor portions of the fifth nerve may be affected separately or conjointly. The motor portion, however, is rarely involved alone. Paralysis may result from softening or patches of sclerosis (tabes) in the pons, from tumors, exudations or traumatic lesions at the base of the brain, from caries of the osseous canals, from certain wounds of the face or mouth, or, very rarely, from peripheral neuritis. Syphilis is occasionally the important factor. The motor nuclei of the nerve may be involved in bulbar paralysis.

Paralysis of the *sensory root* of the trigeminus, if total, causes anesthesia in areas of the skin corresponding to the distribution of the nerve (temple, cheek, external part of the nose and lips; insensibility of the mucous membrane and of the eye, nose, tongue and mouth on the affected side; impairment of taste on the corresponding side of the tongue; abolition of the superficial reflexes; and deficient lachrymation, with dryness of the nasal cavities, and, in consequence, diminished sense of smell. Ulceration of the cornea is not uncommon, especially when the lesion involves the Gasserian ganglion or the nerve anterior to it. Whether this neuro-paralytic ophthalmia, as it is called, is due to paralysis of special trophic fibers in the fifth pair, to an irritable condition of the injured nerve, or to deleterious influences from without acting upon a tissue deprived of sensibility and reflexes is still a mooted question. Ulceration of the mouth and loosening of the teeth less frequently occur.

Herpes, especially in the area supplied by the ophthalmic division of the nerve (herpes zoster ophthalmicus) is also common in lesions of the Gasserian ganglion and likely to be followed by refractory neuralgia. Finally, vasomotor disturbances, sensations of heat or cold, or of stiffness in the affected parts, and imperfect movement of the masticatory muscles are sometimes noted when the anesthesia is complete.

Neuralgia of the trigeminal nerve is described on p. 933.

Destructive lesions of the *motor branch* of the trigeminus cause paralysis of the muscles of mastication—masseter, temporal and pterygoids. In bilateral paralysis chewing is impossible. The affected muscles undergo atrophy and ultimately yield the reaction of degeneration. Irritative lesions of the portion of the cerebral cortex in relation with the fifth nerve give rise to spasm of the masticatory muscles.

## THE SEVENTH OR FACIAL NERVE

**Facial Spasm.**—Spasm of the muscles supplied by the facial nerve is common. It is usually clonic. In many instances the cause is not obvious. In some cases the spasm is due to tumor or other irritative lesion in the facial center of the cerebral cortex, and is the initial feature or the chief manifestation of a Jacksonian convulsion. In other cases peripheral irritations in the eye, mouth or nasopharynx seem to be responsible for the clonic contractions. In some instances peripheral facial paralysis (Bell's palsy) is preceded by muscular twitchings and occasionally twitchings again occur when recovery from the paralysis is nearly complete. Cases of painful facial spasm, relieved by destroying the geniculate ganglion, have been reported by Cushing.[1]

[1] Amer. Jour. Med. Sci., Aug., 1920.

Finally, facial contractions of grimacing character are frequently of psychogenic origin and constitute so-called *tic convulsif* (see p. 1023).

Wave-like fibrillary contractions of the facial muscles (myokymia) occur in many organic and functional nervous diseases.

**Facial paralysis** may be brought about by destructive lesions, such as hemorrhage, softening, gumma or tumor, involving the lower third of the motor area of the *cerebral cortex* or the fibers in the *peduncles* or *pons* that convey facial-motor impulses; by lesions affecting the *nucleus* of the facial nerve in the pons, such as occur in bulbar palsy and occasionally in acute anterior poliomyelitis, chronic anterior poliomyelitis, and syringomyelia; by lesions involving the *peripheral fibers of the nerve* (a) at the base of the brain between the pons and the entrance into the temporal bone, (b) in the petrous portion of the temporal bone, or (c) outside of the stylomastoid foramen.

*Etiology of Peripheral Facial Paralysis.*—The facial nerve may be involved alone or with other cranial nerves in various processes at the base of the brain, such as syphilitic or other tumors, meningeal exudations, and fractures of the skull. Owing to its intimate relation to the temporal bone, the nerve is not rarely affected also in inflammation of the middle ear, in caries of the aqueduct, and in operations on the accessory cavities of the ear. Less frequently facial paralysis can be traced to parotitis, to swelling of the cervical lymph-nodes, or to traumatic injury of the facial nerve. General infections, such as diphtheria and influenza, and chronic intoxications, such as may be produced by alcohol or lead or occur in diabetes, are responsible for a few cases. Herpes zoster of the cephalic extremity, due to inflammation of the geniculate ganglion (herpes otiticus) or of this body and the Gasserian ganglion (herpes facialis) is an occasional etiologic factor. In a large proportion of all cases, variously estimated at from 25 per cent. (Thomas[1]) to 75 per cent. (Huebschmann[2]), there is no discoverable cause for the paralysis other than exposure to cold or draught on the face. Such cases are frequently spoken of as "rheumatic," but there is no evidence that any relation exists between facial paralysis and rheumatism. In some instances, at least, transient acute inflammation of the middle ear seems to be the primary affection. For some unknown cause, possibly owing to congenital narrowing of the stylomastoid foramen (Despaigne[3]), certain persons are especially disposed to facial palsy and, moveover, recurrence of the disease on the same or the opposite side is noted in from 3 to 7 per cent. (Bernhardt[4]) of the cases. Arkwright[5] reports 6 cases in two families and Throckmorton[6] the occurrence of the disease in members of three generations of direct descendants. In a few instances recurrent facial paralysis seems to have been an accompaniment of migraine (facioplegic migraine).

Congenital facial palsy is comparatively rare. It is usually caused by pressure on the nerve by forceps or by the bony pelvis of the mother, although cases have been described in which it was the result of a developmental defect.

Bilateral facial paralysis may occur in the course of multiple neuritis or result from middle ear disease or exposure to cold, but it is usually due to a lesion in the pons or at the base of the brain.

*Symptoms.*—The affected side is flaccid and expressionless; the natural creases are effaced; and the corner of the mouth droops. The eye can be

[1] Jour. Amer. Med. Assoc., 1898, No. 21.
[2] Neurol. Centralbl., Nov. 15, 1894.
[3] Thèse de Paris, 1888.
[4] Neurol. Centralblat, 1899, xviii, 98.
[5] Lancet, Jan. 23, 1904.
[6] Jour. Amer. Med. Assoc., Oct. 3, 1914.

only partly closed, the lower lid is lax, the palpebral fissure is abnormally wide (lagophthalmus), and tears flow over the cheek. Conjunctivitis often supervenes. Every effort of the facial muscles, as in laughing, frowning or talking, accentuates the deformity. On attempts at closing the eyelids forcibly the eyeball is rotated upward and outward. This phenomenon, first described by Bell, is ascribed to an associated movement of the globe, automatically produced through the muscles supplied by the third nerve. Owing to paralysis of the muscles about the mouth, saliva frequently trickles out at the side, food tends to collect between the cheek and the teeth, and the performance of such acts as whistling and blowing is rendered difficult or impossible.

The position of the tongue varies. On account of the asymmetry of the face it often appears to deviate toward the paralyzed side. Occasionally, it is protruded toward the healthy side, probably from an unconscious effort to keep it in the middle of the crooked mouth (Hitzig). In some cases, owing to paralysis of the chorda tympani, the sense of taste is affected in the anterior two-thirds of the tongue on the paralyzed side. Anomalies in the secretion of saliva, of sweat, and of tears may also be noted. Disturbances of hearing are common, but they are usually due to coexistent aural disease. Paralysis of the stapedius, however, may induce abnormal acuteness of hearing, because, as Lucæ pointed out, when the tensor tympani (innervated by the trigeminus) is no longer opposed, the tympanic membrane becomes more tense and the pressure in the labyrinth greater. Patients not rarely complain of pain about the ear and in the neck. This may depend upon otitis media, involvement of the sensory fibers of the facial nerve, or, in cases with herpes, to inflammation of the geniculate ganglion.

The electric excitability of the muscles is usually altered in peripheral facial paralysis. In mild cases there is simply diminished faradic contractility with, perhaps, slightly increased galvanic contractility, but in severe cases there is a partial or complete reaction of degeneration. When the lesion is nuclear or infranuclear, and recovery does not ensue, atrophy and contractures occur in the paralyzed muscles and ultimately the mouth, instead of being drawn, as at first, toward the healthy side, may be drawn toward the paralyzed side. In some cases when recovery is almost complete every movement of the mouth causes slight winking of the eye on the side that has been affected or closure of the eye causes a slight movement of the corresponding angle of the mouth. These associated movements are probably to be ascribed to misdirected regeneration of the nerve-fibers.

In bilateral facial paralysis (*diplegia facialis*) the face remains expressionless, like a mask, under all emotions, but there is no distortion of the features.

*Diagnosis.*—As the recognition of the paralysis itself presents no difficulty, the chief points to be determined are the location of the lesion and the nature of the lesion. In cases of *central or supranuclear paralysis*, the orbicularis palpebrarum and the muscles of the forehead, partially or completely, escape and even those about the mouth, although immobile under voluntary efforts, are usually more or less responsive to the emotions; the secretory and taste functions are not affected, the reflexes are intact, neither atrophy nor electric changes occur in the affected muscles, and there is usually an accompanying hemiplegia. In *nuclear lesions* there is, as a rule, bilateral paralysis of the face and coincident involvement of nerves emanating from adjacent nuclei. When the lesion is *basal between the brain* and *the auditory foramen* other cranial nerves, notably the sixth and eighth, are frequently implicated with the facial, and crossed paralysis (hemiplegia of the opposite half of the body) is sometimes observed from pressure exerted upon the pons. When

the nerve is involved *in the Fallopian canal* hearing is generally disturbed, salivary secretion is often diminished, and, unless the lesion is above the geniculate or below the branching of the chorda tympani, there is loss of taste in the anterior two-thirds of the paralyzed half of the tongue. When the lesion is above the point where the stapedius nerve branches off the disturbance of hearing may take the form of hyperacusis with annoying tinnitus.

When the lesion is *external to the stylomastoid foramen* (*Bell's palsy*) there is complete paralysis of the facial muscles, including the frontalis and orbicularis palpebrarum, as in other infranuclear forms of the disease, but hearing and taste remain normal.

In regard to the exact cause of the paralysis, consideration of the etiologic factors, such as exposure to cold, aural disease, traumatism, syphilis, etc., will usually lead to a correct opinion.

*Prognosis.*—The prognosis of facial paralysis depends upon the cause and the severity of the nerve injury. Recovery rarely occurs in supranuclear or nuclear lesions or those at the base of the brain, unless syphilis is the etiologic factor. The course of the paralysis in aural disease depends upon the curability of the latter. When the cause of the paralysis is exposure to cold or an acute otitic catarrh the outlook is, as a rule, favorable. It can often be determined definitely by data obtained from electrical examination. If at the end of a week or ten days the electrical excitability of the affected muscles is normal or nearly so recovery may be expected within a month. If however, faradism, even with a strong current, gives no response and galvanism gives but a slow, feeble response, recovery is not likely to occur for several months, and may never occur.

*Treatment.*—The cause should be ascertained, and, if possible, removed. In paralysis of central origin little can be done except in syphilitic cases. In middle ear disease treatment should be directed to that condition. When the paralysis is the result of cold and the patient is seen early a blister may be applied behind the ear. Antipyrin, with a mild salicylic compound, such as aspirin, will be found useful in relieving pain. Later, after the lapse of a fortnight, electric treatment should be instituted, that current being used which excites the greatest contraction with the least pain. Massage is also effective. Even after the occurrence of contractures it tends to lessen the feeling of stiffness in the face. If at the end of a year there is no indication of returning power surgical aid may be invoked. Very satisfactory results have been obtained in some instances by anastomosing the facial nerve with the spinal accessory or the hypoglossal, especially with the latter.[1]

## THE EIGHTH OR AUDITORY NERVE

Disease of the cochlear portion of the eighth nerve causes disturbances of hearing, usually deafness or tinnitus aurium. Deafness may result from a lesion of the cochlear nerve itself or some disease of the ear affecting the peripheral fibers of the nerve. If the vibrations of a tuning fork cannot be recognized when the instrument is held near the ear, but are heard when the handle rests on the temporal bone, it may be inferred that the deafness depends upon middle-ear disease and not upon an affection of the labyrinth or of the nerve itself. *Nervous deafness* may result (1) from morbid processes within the labyrinth (inflammation, hemorrhage, leukemic infiltration, etc.); (2) from defective development of the acoustic nerve, which is the chief cause

[1] Ballance and Stewart, Brit. Med. Jour., May 2, 1903; Taylor and Clark, Jour. Amer. Med. Assoc., Mar. 24, 1906; Sharpe, Jour. Amer. Med. Assoc., May 11, 1918.

of deaf-mutism; (3) from lesions at the base of the brain involving the auditory nerves, such as tumors, syphilitic exudations, fractures of the skull, etc.; (4) from atrophy of nerve, due to tabes dorsalis, paretic dementia, or senility; (5) from tumor of the nerve itself; (6) very rarely from involvement of the nerve in the course of polyneuritis (Strümpell, Alt, Meyer); (7) rarely from a lesion of the sensory portion of the internal capsule; (8) rarely from cortical lesions of both temporal lobes; (9) rarely from hysteria. The eighth nerve, of all the cranial nerves, is most frequently affected in syphilis and is most frequently the seat of new growths.

**Tinnitus aurium** depends upon irritation of the auditory portion of the eighth nerve. It may be due to (1) any form of ear disease (cerumen in the auditory canal, otitis media, labyrinthine hemorrhage, sclerosis of the internal ear, etc.); (2) disturbances of the cerebral circulation (arteriosclerosis of the brain, hyperpiesis, anemia, intracranial aneurysm); (3) certain intoxications (cinchonism, salicylism); (4) lesions affecting the auditory paths between the nuclei in the brain stem and the temporal cortex; (5) certain functional diseases of the nervous system (hysteria, traumatic neurosis, epilepsy).

The vestibular nerve with its end organs in the semicircular canals is the chief sensory tract for conveying to the brain those impressions from the periphery which acquaint the individual with the position of his body in space (orientation). Impressions entering the brain through this channel also exercise, through the medium of the cerebellum, a powerful influence upon the centrifugal impulses or muscular innervations necessary for the maintenance of equilibrium and an erect posture. Other centripetal stimuli concerned in preserving equilibrium reach the cerebellum from the eye (optic nerve) and the muscles (sensory tracts of the spinal cord), but these are apparently less important than those coming from the semicircular canals through the vestibular nerve. Affections of this nerve, therefore, are productive of marked vertigo, and, if severe, of staggering and reeling.

**Vertigo** may be defined as a sensation of defective equilibrium and of motion in which the patient himself or surrounding objects appear to be in a state of oscillation or rotation. When severe, it is usually attended by marked mental distress, a feeling of faintness, profuse sweating, nausea and vomiting. It is the result of many diverse conditions, among which the following are the most important.

1. *Disease of the Ear.*—Dizziness may occur in any affection of the ear—otitis media, inflammation of the Eustachian tube, accumulations of wax in the external canal, or furunculosis. It is especially marked in lesions of the labyrinth, constituting when it arises from this cause, the chief symptom of the syndrome known as Ménière's disease (*q. v.*).

2. *Organic Disease of the Brain.*—Vertigo occurs with tumors of the brain in all locations, but it is especially common with growths affecting the cerebellum and pons. It often attends also intracerebral hemorrhage, embolism or thrombosis, syphilitic exudations at the base of the brain, tabes dorsalis, paretic dementia, and disseminated sclerosis.

3. *Disturbances of the Cerebral Circulation.*—Vertigo occurs in all forms of severe anemia. If the cause does not act too precipitously it nearly always precedes syncope. Arteriosclerosis, aortic valvular lesions, and myocardial disease frequently excite it. Distressing attacks not rarely form a part of the Stokes-Adams syndrome. Congestion of the brain produced by violent paroxysms of cough, straining at stool, etc. may also cause swimming of the head.

4. *External Ophthalmoplegia.*—By causing a false projection of the retinal images, paralysis of the ocular muscles is likely to excite disturbance of space-

orientation and varying degrees of dizziness. Upon closing the eyes ocular vertigo disappears.

5. *Various Toxemic Conditions.*—Vertigo may be a prodromal symptom of any of the acute infections. It follows the administration of certain drugs in large doses (nitrites) and is a conspicuous feature of poisoning by quinin, coal-tar products, alcohol, tobacco, conium, opium, and narcotics generally. It is often an early symptom in autointoxication resulting from indigestion. It is sometimes a manifestation of uremia or of the deranged metabolism occurring in diabetes. The peculiar affection prevailing at times among the farmers in certain parts of Switzerland and in the northern provinces of Japan, and known in the former country as *paralyzing vertigo* or Gerlier's disease, and in Japan as *kubisagari*, is probably also of infectious or toxic origin. It is characterized by fugitive attacks of giddiness, accompanied by various disorders of vision and paresis of the eye-lids, neck-muscles and extremities. In the intervals the patients are free from symptoms, or after severe attacks may retain a mild degree of ptosis.

6. *Neuropathic Conditions.*—Vertigo is not uncommon in neurasthenia, hysteria, and traumatic neuroses. It is possibly due in these conditions to abnormal excitation of the semicircular canals. The same is true of the dizziness that frequently precedes or replaces the seizures of epilepsy.

*Peripheral Irritation.*—Occasionally, irritation of the peripheral filaments of nerves other than the vestibular gives rise to a reflex form of vertigo. It is possible that the gastric vertigo of Trousseau may in some instances be of reflex origin. In the majority of cases, however, it seems more rational to ascribe the giddiness that attends indigestion to an intoxication. Leube has reported a case of intestinal vertigo in which the dizziness was produced by the presence of fecal matter, gas, or even the palpating finger in the rectum. Laryngeal vertigo was first described by Charcot[1] as *ictus laryngis*. It is usually, though not invariably, observed in the course of tabes. The attacks begin with tickling in the larynx and spasmodic cough, and not rarely culminate in syncope. Irritation of the nasal mucous membrane in rare instances may also excite vertigo.

8. *Certain Unusual Movements of the Body.*—The vertigo which is produced by swinging, rapid rotary movements, rocking of the ship, etc., is probably in part of ocular origin and in part the result of violent excitation of the semicircular canals.

In recent years Bárány's caloric test (syringing with hot or cold water) and rotation test (the rotations being made with aid of special revolving chair) have proved of great value in localizing the lesions responsible for vertigo and nystagmus. By these tests it is almost always possible to decide whether or not the eighth nerve is diseased and to differentiate lesions of the labyrinth from those of the cerebellum.[2]

**Ménière's Disease.**—In 1861 Ménière[3] described before the French Academy of Medicine the case of a young woman who during menstruation was suddenly affected with deafness in both ears, accompanied by vomiting and severe vertigo. Five days later she died and on *post-mortem* examination the only lesion found was hemorrhage into the semicircular canals. The study of this case, in connection with the well known results of animal experimentation, led Ménière to believe that similar clinical pictures and

[1] Gaz. Méd. de Paris, 1876.

[2] For a full consideration of the subject the reader should consult "Equilibrium and Vertigo," by Isaac H. Jones; "The Ear Tests of Bárány in Locating Cerebellar and Other Encephalic Lesions," Randall and Jones, Amer. Jour. Med. Sci., April, 1916.

[3] Gaz. Méd. de Paris, 1861.

others showing sudden and increasing diminution of hearing, with tinnitus aurium and recurring attacks of severe vertigo, were due to hemorrhage or acute inflammatory exudation into the labyrinth. It was soon discovered, however, that symptoms differing only in degree and in manner of appearance from those described by Ménière could arise from chronic affections of the labyrinth, diseases of the middle and external ear, and even functional disturbances of the labyrinthine vessels. To accommodate these clinical variations the terms "Ménière's symptoms" and "vertigo with aural lesions" were introduced, but they have not proved entirely satisfactory, since much discussion has arisen in regard to their proper application. Moreover, it has not been established with certainty that the pathologic findings are always the same in cases corresponding exactly with those described by Ménière himself, because a fatal ending is unusual. It would seem desirable, therefore, to abandon entirely the names "Ménière's disease" and "Ménière's symptoms" in favor of a nomenclature based on anatomical conditions. Certainly, if the former title is retained it should be applied only to the comparatively rare cases in which there is sudden monaural or binaural impairment of hearing, followed by tinnitus and recurring attacks of intense vertigo, culminating in vomiting and perhaps syncope.

Nystagmus may or may not accompany the vertigo. As a rule, the affection shows a progressive tendency, the attacks becoming more frequent and severe, until finally the patient is incapacitated for work. With the occurrence of complete deafness, however, the distressing dizziness and tinnitus often cease. Occasionally the labyrinth is destroyed at once and the first attack of vertigo is the last. A fatal issue is rare, although it did occur in Ménière's case.

The results of *treatment* are far from being satisfactory. Patients should avoid excitement, both mental and physical, and should refrain from alcohol and tobacco. Quinin, originally recommended by Charcot, is perhaps the drug of greatest efficacy. It may be administered in doses of 2 or 3 grains (0.13—0.2 gm.) several times a day. There is no need to induce cinchonism. Bromids and iodids may give good results. Pilocarpin (1/6 of a grain—0.01 gm.) hypodermically, every other day, for two or three weeks, sometimes proves beneficial. Counter-irritation behind the ear has been recommended, but it rarely affords relief.

## THE NINTH OR GLOSSOPHARYNGEAL NERVE

The glossopharyngeal nerve contains both sensory and motor fibers, and these are distributed to the posterior portion of tongue (taste and common sensibility), to the middle ear (sensibility), to the pharynx (sensibility and motion), and to the parotid gland. The nerve may be involved with other cranial nerves in disease of the medulla, such as bulbar palsy, and in various lesions at the base of the brain. Isolated glossopharyngeal paralysis has been described. Anesthesia of the throat, loss of taste in the posterior third of the tongue, difficulty in swallowing and imperfect phonation are the symptoms attributable to lesions of the ninth nerve, but to what extent coincidental involvement of the vagus and hypoglossal nerves shares in the production of these disturbances cannot be determined in individual cases, as the peripheral fibers of all three nerves are so intimately mingled.

## THE TENTH OR PNEUMOGASTRIC NERVE (THE VAGUS)

The nuclei of the vagus are not rarely affected with those of the glossopharyngeal nerve in bulbar palsy and other diseases implicating the medulla

oblongata, such as tabes, syringomyelia, and disseminated sclerosis. The nerve-roots may be involved at the base of the brain in neoplasms, meningeal exudations, hemorrhages, etc. In the neck the trunk of the nerve may be damaged in consequence of traumatism, surgical operation, deeply seated tumor, goiter, or carotid aneurysm. Within the thorax the main branch of the nerve, the recurrent laryngeal, is often affected in aneurysm, carcinoma of the esophagus, tumors of the mediastinum and tuberculous or leukemic adenopathies. Occasionally it is compressed by a pericardial or pleural effusion or by an enlarged left auricle (mitral stenosis). Garland and White[1] have analyzed 70 cases of paralysis of the recurrent laryngeal nerve in mitral stenosis. The recurrent laryngeal nerve, with the trunk of the pneumogastric, the hypoglossal (dysphagia) and the sympathetic (myosis), is not rarely involved in tumor of the carotid gland. Roux[2] reports permanent injury of the recurrent laryngeal nerve in 1.2 per cent. of 20,654 operations for goiter.

The fibers of the vagus are sometimes affected in the course of multiple neuritis, the result of acute infections (diphtheria, etc.), beri-beri, or alcoholism.

Irritation of the recurrent laryngeal nerve or of the peripheral endings of the pneumogastric may give rise to *laryngeal spasm*. The latter is responsible for certain forms of spasmodic cough, false croup, laryngismus stridulus, the shrill epileptic cry, and the laryngeal crises of tabes.

Paralysis of the vocal cords may be complete or incomplete, unilateral or bilateral, and may result from a central or peripheral lesion. Laryngeal abductor palsy may be the first indication or for a long time the only conspicuous symptom of such conditions as tabes, cerebrospinal syphilis, aortic aneurysm and carcinoma of the esophagus.

Severing the vagus on one side does not usually cause serious symptoms on the part of the heart or lungs; although it results in permanent palsy of the vocal cord. Irritation of the nerve, however, may cause severe disturbances, such as dyspnea, paroxysmal cough and even complete arrest of the heart. Bilateral vagotomy is followed by tachycardia, dyspnea and congestion and inflammation of the lower lobes of both lungs. Certain drugs have a selective action on the vagus; thus, aconite and digitalis stimulate the cardiac branches, and belladonna depresses the fibers distributed to the lungs, heart and digestive tract. Functional depression of the vagus, especially of the laryngeal branches, is not uncommon in hysteria.

**Vagotonia.**—According to Eppinger and Hess and others, certain individuals suffer from a group of symptoms which are the result of excessive sensitization of the autonomic nervous system, consisting of the vagi, oculomotor and pelvic nerves. These symptoms, which have been associated with a disturbance of one or several of the endocrine glands, occur in various conditions, such as neurasthenia, epilepsy, hyperthyroidism, peptic ulcer, etc., and modify, more or less, the clinical pictures. The vagotonic syndrome comprises myosis, hot flushes, free perspiration, cold, bluish hands, dermatographia, infrequency of the pulse, low blood-pressure, eosinophilia, and a tendency of spatm of the gastro-intestinal muscles, as shown by esophagismus, cardiospasm, pylorospasm, spastic constipation and mucous colic. The symptoms are favorably influenced by atropin, which depresses the autonomic system and to a less extent by epinephrin, which stimulates the sympathetic system, and are aggravated by pilocarpin. Vagotonia is the antithesis of sympathicotonia, which is characterized by mydriasis, dryness

[1] Arch. of Int. Med., Sept. 15, 1920.
[2] Correspond.-Bl. f. Schweiz., 1917, No. 48.

of the skin, frequent pulse, high blood-pressure, eosinopenia, and lessened gastrointestinal tonus.[1]

## THE ELEVENTH OR SPINAL ACCESSORY NERVE

The spinal accessory nerve, which innervates the sternocleidomastoid muscle and, in part, the trapezius, may be damaged by traumatic injuries involving the neck, by diseases of the upper cervical vertebræ, or by tumors, glandular enlargements or abscess in the neck. Less frequently it is implicated in tabes, syphilis, meningitis, and other processes affecting the cervical cord. Inflammation of the nerve from infectious diseases or exposure to cold is also occasionally met with.

Lesions of the spinal accessory nerve usually result in paralysis of one or both of the above-named muscles. In unilateral paralysis of the sternocleidomastoid the chin is slightly elevated and directed toward the affected side and there is difficulty in turning the head to the opposite side. Rotation is not impossible, however, as the deep muscles at the back of the neck are brought into play. If the paralysis is prolonged torticollis may ensue from contraction of the healthy muscle. In bilateral paralysis there is difficulty in turning the head to either side and the lateral regions of the neck are flattened. In unilateral paralysis of the trapezius the scapula on the affected side is depressed and prominent, elevation of the shoulder is interfered with, and there is difficulty in drawing the scapula toward the spinal column and in raising the arm anteriorly to the horizontal position. In paralysis of both trapezii the shoulders droop, the clavicles are abnormally prominent, and the back is strongly arched.

**Torticollis or wry-neck,** although not always caused by irritation of the spinal accessory nerve, may be referred to in this place. *Fixed torticollis* results from persistent contraction or actual shortening of the cervical muscles, particularly the sternocleidomastoid and the trapezius. The head is drawn to one side and so rotated that the occiput approaches the shoulder, and the chin is directed toward the opposite side. In chronic forms the deformity is often increased by defective development of the upper half of the face, bending of the cervical spine, and a compensatory lateral curvature in the dorsal region. Attempts at forcible correction of the distortion give rise to considerable pain.

Fixed torticollis may be congenital, the result of mal-development in fetal life or malposition *in utero*. Not infrequently, however, the congenital form is due to injury of the muscles at birth by forceps or the manipulations of the accoucher. Traumatic cases are also met with in later life. In some instances the cervical muscles of one side are shortened by the shrinking of cicatrices, the result of extensive burns or abscesses of the neck. In other cases the muscular contraction is spastic and can be traced to disease of the cervical vertebræ, to enlargement of the cervical lymph-nodes, to middle ear disease, or to some more remote peripheral irritation. Hysterical contracture of the muscles which rotate the head is not very rare. Compensatory torticollis is met with in cases of lateral curvature and sometimes as a sequel of unilateral visual defects (*torticollis oculaire*). In unilateral paralysis of the sternocleidomastoid, wry-neck may arise from contraction of the healthy muscle on the opposite side. Finally, an acute form of the affection, the familiar "stiff neck," often results from exposure to cold.

*Spasmodic Torticollis.*—This term is applied to intermittent spasmodic contractions or twitchings of the muscles of the neck, especially the sterno-

[1] For a more complete consideration of the subject the reader is referred to articles by Spitzig and Wolfsohn, Journal of Amer. Med. Assoc., Jan. 31, 1914, and May 16, 1914.

cleido-mastoid and trapezius. If the sterno-cleido-mastoid only of one side is affected the occiput is pulled toward the shoulder and the chin is drawn toward the opposite side and elevated. If both sterno-cleido-mastoids are involved the head is jerked first to one side and then the other. When the trapezius is implicated the head is drawn backward and toward the diseased side, the shoulder is raised, and the scapula is brought nearer the spine. The spasms occur in paroxysms, which, as a rule, become more frequent, more intense and more prolonged as time passes. They usually cease during sleep and are aggravated by mental or physical excitement. In severe cases the movements may extend to all the muscles of the neck, to those of the shoulder, and even to those of the arm. More or less discomfort, if not actual pain, usually attends them and sometimes the distress is so great that the patient is unable to work. Occasionally, light pressure upon the chin or upon the head at some point serves to arrest temporarily the spasm.

The etiology of spasmodic torticollis is obscure. In some instances the affection is definitely hysterical, and rarely it appears to be reflex, but in the great majority of cases no coarse lesion of the nerve-centers or peripheral focus of irritation can be discovered. It usually occurs in persons between 25 and 50 years of age who are innately neuropathic, and probably constitutes in many instances a psychogenous tic (torticollis mental) or a psychomotor disturbance in which muscular contractions, originated, perhaps, by some trivial peripheral irritation, are repeated automatically through lack of inhibition.

The treatment of spasmodic torticollis does not often yield satisfactory results. In the main, it is that of the tics (see p. 1023). Tincture of gelsemium in doses gradually increased from 5 minims (0.3 mil) to 20 minims (1.3 mils), three times a day, its effects being carefully observed, sometimes affords temporary relief. Resection of the spinal accessory nerve and cross cutting of the muscles themselves have been tried in severe cases, but usually these operations have arrested the spasm only for a time.

## THE TWELFTH OR HYPOGLOSSAL NERVE

The hypoglossal nerve is a motor nerve for the muscles of the tongue. Lesions affecting it are most commonly supranuclear and comprise tumor, abscess, hemorrhage, softening, etc. at any point in the course of the nerve between the center in the lower part of the precentral convolution and the nucleus in the floor of the fourth ventricle. Nuclear paralysis is usually bilateral and occurs in bulbar palsy and sometimes in tabes and syringomyelia. Infranuclear involvement is comparatively rare, but occasionally occurs in basilar processes, such as meningitis, fractures, etc., in disease of the upper cervical vertebræ, and in wounds in the neck.

The chief symptom of injury to the hypoglossal nerve is interference with the movements of the tongue. When the paralysis is unilateral the tongue on being protruded deviates toward the paralyzed side, owing to the unopposed action of the healthy geniohyoglossus muscle. Disturbances of sensation are absent and in many cases speech, mastication and deglutition are but little affected. In nuclear and infranuclear disease the paralyzed half of the tongue shows fibrillary twitchings and is flabby, wrinkled, and wasted. In bilateral paralysis, which is usually attributable to a bulbar affection, the tongue can be protruded but slightly, if at all, the whole organ is atrophic, and speech, mastication, and deglutition are seriously affected.

Paralysis of supranuclear origin is generally accompanied by hemiplegia,

while that resulting from disease of the nuclei or roots of the nerve as they emerge from the medulla is almost always attended by paralysis of the adjacent glossopharyngeal and pneumogastric nerves. In 1903, Panski[1] collected 40 cases of isolated hypoglossal palsy due to peripheral disease or injury.

**Localized spasm of the tongue** (**glossospasm**) is occasionally observed in hysteria, rarely as a result of peripheral irritation arising in the teeth, and still more rarely as result of a circumscribed lesion of the cerebral cortex.

## THE PHRENIC NERVE

The phrenic nerve, the motor nerve of the diaphragm, is derived from the third, fourth and fifth cervical nerves. It may be involved in (1) fracture or caries of the cervical vertebræ, cervical spinal meningitis, or disease of the cervical spinal cord; in (2) penetrating wounds of the neck; in (3) tumor or aneurysm within the thorax; or, more frequently, with other nerves, in (4) polyneuritis, due to diphtheria, alcoholism, beri-beri, or lead-poisoning.

Unilateral paralysis of the phrenic nerve may cause but little subjective disturbance. Dyspnea may or may not be present. Inspection shows absence of Litten's diaphragm phenomenon on the affected side and fluoroscopic examination, unilateral immobility of the diaphragm during inspiration. The deficient action of the diaphragm favors the occurrence of pneumonia and adds enormously to the gravity of the disease when it does occur. Bilateral phrenic paralysis is always a serious occurrence and in young children almost invariably fatal within 2 or 3 days. The breathing is dyspneic and wholly intercostal in character. Protrusion of the upper abdomen during inspiration is absent and may be replaced by retraction. The vesicular murmur at the base is feeble, and fluoroscopic examination reveals absence of diaphragmatic movements. Hypostatic congestion of the lungs or actual pneumonia is very likely to occur.

## THE BRACHIAL PLEXUS

The nerve roots forming the brachial plexus—the four lower cervical nerves and the first thoracic nerve—may be damaged (1) by diseases involving the cervical cord, meninges or vertebræ; (2) by trauma, such as a wound, a fall upon the shoulder, dislocation or fracture of the head of the humerus, pressure in the axilla by a crutch, excessive torsion, extension or abduction of the arm, and overexertion in occupation; (3) by tumor or abscess in the neck or axilla; (4) by neuritis due to infection or intoxication, or the extension of an inflammatory process in a contiguous part, such as the shoulder-joint.

**Brachial birth-palsy** and so-called **anesthesia paralysis** are also of traumatic origin, although it is possible that in the latter the toxic action of the anesthetic may sometimes be an auxiliary factor.

Paralysis from the above-mentioned causes may affect the entire plexus or may be limited to isolated nerves. It presents every possible degree of severity, and is often unequal in different muscles innervated by the same nerve. With the paralysis there are frequently the sensory disturbances (pain, paresthesia, anesthesia), the changes in electrical excitability ranging from simple diminution of contractility to well developed reactions of degeneration, the atrophy of the affected muscles, and the vasomotor anomalies described in the section on neuritis (q.v.).

[1] Neurolog. Centralbl., Aug., 1903.

Total brachial paralysis is comparatively infrequent. It is manifested by a loss of function, more or less complete, in all the muscles of the arm. Partial brachial paralysis may assume one of two forms, the superior or inferior.

**Superior or Upper-arm Form (Duchenne-Erb Paralysis).**—This form, which involves the fifth and sixth cervical nerves, is not rarely seen at birth as a result of stretching of the brachial plexus or tearing of the shoulder-joint capsule or a subluxation of the joint during a difficult labor, and it sometimes occurs in adults as a result of trauma affecting the supraclavicular region or the shoulder-joint. The paralysis is usually limited to the deltoid, biceps, brachialis anticus, supinator longus, but it may also affect the supraspinatus and infraspinatus. The patient cannot raise the arm or flex it at the elbow. The whole member hangs to the side limp, with the forearm extended and pronated. The movements of the hand are retained but the fingers are flexed. Sensation is sometimes impaired on the outer side of the arm and forearm. The affected muscles are flaccid and soon show considerable atrophy, and unless power is restored the injury results in a lack of growth in the whole limb or shoulder-girdle. The prognosis depends upon the character and severity of the lesion. In birth-palsy due to stretching of the plexus recovery within a few months or a year is the rule. If there is a luxation of the shoulder-joint this should be corrected as soon as possible, otherwise recovery is likely to be incomplete. In long-standing cases a nerve anastomosis, tendon transplantation or arthrodesis may be indicated, according to the exact conditions.

**Inferior or Lower-arm Form (Klumpke's Paralysis).**—This form is due to a lesion of the eighth cervical and the first thoracic roots, the result of compression by a tumor, disease of the lower cervical or upper thoracic vertebræ, or trauma. It is characterized by atrophic paralysis of the small muscles of the hand, the thenar and the hypothenar eminences and the interossei (ulnar nerve), anesthesia or hypesthesia of the radicular type along the inner side of the hand and forearm, and, in case the sympathetic fibers from the eighth cervical and first thoracic roots are involved, by certain oculomotor symptoms, namely, myosis, narrowing of the palpebral fissure, and slight retraction of the eye-ball on the side of the injury. Eventually the characteristic *main en griffe* deformity, or claw-like hand, may be produced.

*Diagnosis.*—Peripheral brachial monoplegia may be distinguished from *central brachial monoplegia* by the early appearance of atrophy and electrical changes, and by the absence of cerebral symptoms. The mode of onset, the fixity of the paralysis, the occurrence of trophic and electrical changes, the decrease or absence of the tendon-reflexes, and the characteristic limitation of the sensory disturbances to the distribution of the nerves will serve to differentiate it from *hysterical palsy of the arm.*

Syringomyelia, progressive spinal muscular atrophy, and hypertrophic cervical pachymeningitis may present difficulties in diagnosis, particularly if the brachial paralysis is bilateral. The appearance of sensory disturbances in bands or zones corresponding to the spinal-cord segments, a marked dissociation of sensation—abolition of pain and temperature senses with retention of contact sense—severe trophic changes in the skin and joints, fibrillary twitchings in the affected muscles, curvature of the spine, and spastic symptoms in the legs are in favor of *syringomyelia.* In *progressive muscular atrophy* no definite etiologic factor can be ascertained and spontaneous pain and objective sensory disturbances are absent. Before the occurrence of cord symptoms it may not be possible to distinguish *hypertrophic pachymeningitis of the cervical region* from bilateral brachial neuritis.

Brachial neuritis is often confused with *arthritis of the shoulder-joint* and

with *subacromial bursitis*. In these more common conditions, however, pain is usually most marked in the region of the shoulder, although it may extend downward as far as the fingers, there is much greater disability in shoulder movements than in neuritis, neither the cords of the plexus nor the nerve-trunks are tender, neither surface hyperalgesia nor tactile anesthesia is present, and the deep reflexes of the arm are not diminished.

**Injury of the Brachial Plexus by Cervical Ribs.**—In some instances supernumerary cervical ribs produce symptoms referable to an injury of the brachial plexus or of the subclavian artery. The nervous symptoms are much more frequent than the vascular and are due to stretching of the lower cords of the plexus by the lifting action of the rib in inspiration. Pain radiating from the neck down the arm, numbness and tingling or a sensation of coldness, especially in the area of ulnar distribution, and a feeling of stiffness or weakness in the limb are the most common phenomena. Muscular exertion increases the suffering and most patients are worse in winter than in summer. In the course of time atrophy may occur in the muscles of the forearm and hand.

Owing to compression or bending of the subclavian artery in the angle between the rib and the scalenus anticus, vascular disturbances often arise. Thus, there may be marked pulsation in the neck, sometimes with a thrill and bruit, strongly suggestive of aneurysm. Not infrequently the radial pulse on the affected side is much weaker than on the other side, especially when the arm is dependent, and occasionally, owing presumably to a thrombus in the vessel, no pulse whatever can be obtained in the forearm or arm. As a result of the ischemia the limb may be cold and livid. Gangrene, however, is rare, although, according to Keen,[1] it has been observed in the finger-tips in at least seven instances. Scoliosis, with the convexity usually toward the side of the anomaly, was present in 22 of 61 cases collected by Schönebeck.[2] It is noteworthy that in several of the recorded cases defects in the central nervous system, especially syringomyelia, also existed.

The symptoms are usually unilateral and on the side of the larger or more highly placed rib. As a rule they do not appear before ossification of the rib occurs, which is in early adult life. Somewhat frequently the extra bone can be felt projecting above the clavicle, but to reach a positive diagnosis a radiographic examination must be made. Removal of the offending rib is the only treatment that is likely to prove effectual.

**Posterior (Long) Thoracic Nerve.**—This nerve is formed by fibers of the fifth, sixth and seventh cervical nerves and supplies the serratus magnus muscle. It may be damaged by contusions or wounds affecting the supraclavicular fossa, by operations upon the axilla, by pressure of heavy loads upon the shoulder, by violent movements of the arm, and by neuritic processes resulting from infectious diseases or intoxications. Paralysis of the nerve produces a characteristic deformity. When the arm is put forward the scapula is rotated in a direction opposite to that in which the serratus itself would rotate it and is made to project from the thorax like a wing. There is also difficulty in raising the arm above the horizontal position. Neuritic pains frequently accompany the paralysis.

**Circumflex Nerve.**—This nerve, which supplies the deltoid and teres minor muscles, the shoulder-joint, and the skin over the deltoid, is sometimes paralyzed in injuries of the shoulder-joint, by compression of a crutch-head, or as a result of neuritis following a general infection or intoxication. The symptoms of paralysis are inability to raise the arm, atrophy of the deltoid

[1] Amer. Jour. Med. Sci., Feb., 1907.
[2] Inaugural Dissertation, Strassburg, 1905.

muscle, relaxation of the ligaments of the shoulder-joint, and an area of anesthesia in the upper and posterior part of the arm. Pain is usually present at the onset of the symptoms.

**Musculospiral Nerve.**—Owing to its exposed position this nerve is very frequently injured. Paralysis may ensue from a direct blow or other violence, from pressure of the head upon the arm during sleep or a drunken stupor, from compression of the nerve during anesthesia, from the application of a tight bandage to the arm, from fracture of the humerus, from pressure in the axilla of a poorly-padded crutch, or even from the deep injection of drugs into the arm. It is often a conspicuous feature also in polyneuritis from various causes, especially lead poisoning.

The chief symptom of complete musculospiral paralysis is loss of power in the triceps, anconeus, brachialis anticus, supinator longus (bracho-radialis) and extensor carpi radialis, which is revealed by wrist-drop, inability to extend the forearm and hand, impairment of supination, and weakness of the hand-grip, the last being due to the loss of resistance normally supplied by the extensors of the wrist. When the nerve is involved in the forearm the triceps, and supinator longus escape. Wasting and electrical changes may ultimately appear in the affected muscles. Sensory disturbances are often absent, but paresthesia, hypesthesia, or anesthesia is sometimes observed on the radial side of the forearm and hand and on the dorsal surface of the thumb.

**Median Nerve.**—This nerve supplies all the flexors on the front of the forearm (except the flexor carpi ulnaris and the ulnar half of the flexor profundus digitorum) both pronators, and in the hand all the muscles that abduct, flex and oppose the thumb, and the two outer lumbricales, which flex the terminal phalanges of the index and middle fingers. It is often injured in wounds, contusions, and fractures involving the forearm, and occasionally it is damaged in occupations that make excessive demands upon the muscles of the hand. When paralysis results from a lesion of the nerve high up it is manifested by difficulty in pronating and flexing the forearm, by inability to flex the second and third phalanges of the index and middle fingers, by the loss of abduction, flexion, and opposing function of the thumb, and frequently by disturbances of sensation on the radial side of the palm, the palmar surface of the thumb, both palmar and dorsal surfaces of the index and middle fingers and the radial side of the ring finger. When the lesion is just above the wrist, which is often the case, the muscles of the thumb only are paralyzed. Severe injuries of the nerve are usually accompanied by atrophy of the thenar muscles and trophic changes in the skin and nails.

**Ulnar Nerve.**—This nerve supplies in the forearm the flexor carpi ulnaris, and the ulnar half of the flexor profundus digitorum, and in the hand the muscles of the hypothenar eminence, the two ulnar lumbricales, the interosseous muscles, and the adductor pollices. It may be injured by blows or wounds, especially at the elbow, by compression during sleep or prolonged anesthesia, by the pressure of a crutch in the axilla, or by overuse of the small muscles of the hand in certain occupations. Occasionally it is dislocated or thrown out of its groove behind the internal condyle by direct traumatism or violent muscular exertion.

In complete paralysis of the ulnar nerve the movements of the hand are much impaired, the fingers cannot be separated or brought together, the first row of phalanges cannot be flexed, nor the last two rows extended, the little finger is almost useless, the thumb cannot be adducted, and there is disturbance of sensation over the entire little finger, the ulnar side of the ring finger, and the inner border of the hand. In severe cases the hypothenar

eminence is flattened, the interosseous spaces are sunken, and, owing to the unopposed action of the flexors and common extensor, the claw-hand—the *main en griffe*—is produced.

Paralysis of the ulnar nerve sometimes occurs in adults as a result of an injury to the elbow-joint in childhood (tardy paralysis). The condition is manifested by weakness, muscular atrophy, paresthesia and hypesthesia in the ulnar distribution of the hand and frequently also by a spindle-shaped swelling of the nerve itself. Sherren[1] in 1908 collected from the literature 23 cases and recently Shelden[2] has reported 15 cases, with operation, from the Mayo Clinic.

## THE LUMBAR PLEXUS

The lumbar plexus is composed of the anterior divisions of the twelfth thoracic and four upper lumbar nerves. It supplies the flexors, adductors, and abductors of the thigh, the extensors of the knee, the cremasteric muscle, and the skin of the lower part of the abdomen, scrotum or labium, thigh except the posterior aspect, and inside of the leg and foot. It may be damaged in fractures of the pelvis, wounds or contusions of the groin, dislocations of the hip, diseases of the lumbar vertebræ, abdominal tumors, abscesses of the psoas muscle, or neuritic processes resulting from general infections or intoxications. The obturator and the anterior crural nerves are occasionally injured during parturition.

In paralysis of the **obturator nerve** the patient is unable to cross one leg over the other or to press the knees firmly together. There may be also sensory disturbances on the inner side of the thigh. The pain of the knee complained of in hip-joint disease, cancer of the sigmoid flexure, and obturator hernia is caused by irritation of the obturator nerve.

Paralysis of the **anterior crural nerve** is revealed by inability to flex the thigh at the hip, to extend the leg at the knee, and to perform such acts as walking, jumping, etc., and also by loss of the knee-jerk and by sensory disturbances in the area supplied by the nerve, especially on the inner and anterior surfaces of the thigh and leg and the inner side of the foot.

**Meralgia Paresthetica.**—This symptom-complex, first described in 1895, almost simultaneously by Bernhardt[3] and Roth[4] is characterized by paresthesia, paroxysms of pain, and impaired sensibility over the anteroexternal aspect of the thigh, or region supplied by the external cutaneous nerve. It usually occurs between the ages of 30 and 50, and males are affected thrice as often as females. Persistent slight traumatism, as by a truss or corset, infectious diseases, alcoholism, gout, plumbism, exposure to cold, and pregnancy have been regarded as etiologic factors. In a few instances association with tabes has been noted. The lesion is a mononeuritis.

The symptoms are, as a rule, unilateral. The paresthesia takes the form of numbness, coldness or formication, and is almost constant. The pain, usually described as a burning sensation, is paroxysmal. Occasionally, pressure on the thigh or even friction by clothing is sufficient to excite it. Objective disturbances of sensation—tenderness at a point just below the anterior superior spine of the ileum and diminished sensibility for touch and for heat or cold—are also present. Deep or protopathic sensibility, however, is unimpaired. Complete recovery is not the rule, but it may be

[1] Edinburgh Med. Jour., 1908, xxiii.
[2] Med. Clin. of North America, Sept., 1921.
[3] Neurol. Centralbl., 1895.
[4] *Meralgia Paresthetica;* Berlin, 1895.

attained. The painful attacks usually become less frequent with the lapse of time. Apart from measures directed to the underlying condition, rest, massage, hydrotherapy and faradism are to be recommended. In severe persistent cases neurectomy is advisable. It has been done successfully by Souques, Chipault, Bramwell and others.

## THE SACRAL PLEXUS

The sacral plexus is formed by the lumbo-sacral cord and the anterior divisions of the three upper and part of the fourth sacral nerves. It may be injured in fractures of the pelvis and inflammatory processes, or neuritis of a toxic or infectious origin. Occasionally it is damaged during difficult labor.

**Complete paralysis of the sciatic nerve** is rare. It is shown by an inability to extend the thigh and to flex the leg, by a loss of motion in all the muscles below the knee, and in some cases, also, by anesthesia on the outer aspect of the leg and on the sole and most of the dorsum of the foot.

**Paralysis of the external popliteal** or **peroneal nerve** is manifested by inability to flex the foot dorsally and to extend the first phalanges of the toes. In consequence of the foot-drop and toe-drop the patient in walking lifts the leg abnormally high and throws the foot forward (steppage gait). Anesthesia may be present on the outer aspect of the leg and on the dorsum of the foot, and equinovarus may ultimately develop from overaction of the healthy muscles.

**Paralysis of the internal popliteal nerve** is shown by inability to extend the foot and to flex the toes. Standing on tiptoe is impossible and walking is difficult. There may be sensory disturbances over the back of the leg, outer border of the foot, and the sole. In severe cases a deformity similar to the "claw-hand" may be produced.

**Sciatica.**—This term is applied to pain in the course of the sciatic nerve. In the large majority of cases the pain is merely referred to the nerve, the disease responsible for it being in some closely related structure. In some instances, however, the pain is an expression of actual sciatic neuritis or perineuritis. By far the most frequent cause is a lesion of the lower spine or of the lumbosacral, sacroiliac or hip joint. The lesion itself is usually an arthritis resulting from focal infection, but it may be a new growth or tuberculosis. In other cases the pain is due to compression of the parent plexus within the pelvis by inflammatory exudation, a tumor, hardened fecal matter, or the fetal head in protracted labor. Not an uncommon cause is inflammation of the prostate or seminal vesicles or carcinoma of the prostate. In lesions of the cauda equina there is often pain in the sciatic regions, with anesthesia in root areas, weakness of the sphincters, and gradually increasing paresis in the legs. Syphilis plays a minor rôle, but it may cause sciatica by producing spondylitis or a primary neuritis. Varicose veins in the thigh, especially within the sheath of the sciatic nerve, are an occasional factor.

In a comparatively small proportion of cases sciatica is due to a true neuritis. The basic condition in these cases may be an acute infection, syphilis, alcoholism, diabetes or gout. Sometimes an arthritis of the sacroiliac or hip joint sets up an actual neuritis. Not rarely the cause of the neuritis cannot be ascertained. In some of the obscure cases a fibrositis or perineuritis, with compression of the nerve by adhesions, seems to be responsible for the persistent pain.

Individual attacks of sciatica or exacerbations of pain are often traceable to exposure to cold, to direct pressure by a hard object, such as the sharp

edge of a chair, and to undue fatigue. Sciatica is rare before the age of 21 years and is much less common in women than in men.

*Symptoms.*—The pain may extend along the entire course of the nerve, but frequently it is felt only on the posterior aspect of the thigh, and occasionally it is limited to the outer side of the leg and foot, or even to the back of the knee. Movements of the hip, such as abduction, flexion and external rotation, increase the pain, especially in the arthritic cases, and, as, a rule, when the thigh is flexed the leg cannot be extended without causing severe pain (Lasègue's sign). In standing the patient instinctively flexes the knee and rotates the spine to the sound side. In severe attacks he limps or is unable to walk. In the neuritic type there may be sensitiveness to pressure, and various anomalies of sensation, painful cramps and loss of power may be present. Atrophy of the muscles may also occur in long-standing cases, but in arthritic and radicular sciatica it is confined to the gluteal region. The course of the disease varies. Acute attacks may end in recovery within two or three weeks. Only exceptionally, however, does the patient escape a recurrence. In many cases the condition is essentially chronic and continues with periodic exacerbations for months and years.

*Diagnosis.*—The recognition of sciatica is rarely difficult, but an accurate history and a thorough physical examination are frequently necessary in deciding whether the pain is merely referred to the region of the sciatic nerve or is an expression of a true neuritis. In the latter, movements (except extension of the leg with the thigh flexed) are much less restricted and painful, the nerve itself is often tender, the deep reflexes are diminished, if muscular atrophy is present it is not confined to the gluteal region, and radiographic studies of the lower spine and pelvic joints, rectal and vaginal examinations, and palpation of the seminal vesicles usually yield negative results. With neuritic sciatica the next step in diagnosis is to determine, if possible, the underlying cause, bearing in mind the possible factors, such as focal infection, syphilis, diabetes, etc. Tabes with lightening pains, flat-foot, osteomyelitis, and intermittent claudication are conditions that have sometimes been mistaken for sciatica.

*Treatment.*—The cause must be removed, if possible. In all cases rest is essential. If the symptoms are severe not only should the patient be put to bed, but the movements of the affected limb should be restricted by sand bags or a long hip-splint. Free evacuation of the bowels should be secured in order to deplete the pelvic veins. Irrespective of the cause of the disease, such drugs as the salicylates, acetphenetidin, and cinchophen (atophan), in full doses, are sometimes effective in relieving pain. Morphin is sometimes necessary, but it should be used only as a last resort. Counterirritation is sometimes of service. It is best accomplished by means of dry cups or small blisters along the course of the nerve. In some cases acupuncture acts satisfactorily and in others good results are achieved by directing a stream of hot water down the back of the thigh. High frequency electric currents or static induced currents are sometimes very effective. Massage is contraindicated.

In refractory cases, when no organic abnormalities outside the sciatic nerve are discoverable, injections of normal salt solution into the tissues surrounding the nerve or into epidural space are worthy of trial. Complete or partial relief, often lasting, may be expected in at least one-third of the cases. In perineural injections the fluid (100 to 150 mils) is introduced forcibly at a point 1 inch to the outer side of the junction of the inner one-third and the outer two-thirds of a line drawn from the sacro-coccygeal articulation to the lowest point of the postero-external border of the great

trochanter, the needle being inserted directly downward through the gluteal muscles until the nerve is reached (6–12 cm.), as shown by a sharp, shooting pain down the leg. Owing to their destructive action, injections of alcohol are contraindicated. Epidural injections (50 to 80 mils of salt solution, the first with epinephrin and novocain) are made at the level of the sacro-coccygeal articulation through the foramen sacrale superius.[1] Ott,[2] of the Mayo Clinic, reports that in 34 cases of sciatica without obvious cause the removal of possible foci of infection in 62 per cent., combined with from one to four or five epidural injections, gave a permanent cure in 27 per cent. and permanent relief in 40 per cent.

Arthritic cases will require removal of the infective focus, if this can be discovered, and appropriate orthopedic measures. Cases due to prostatitis or spermatocystitis may require the aid of the genito-urinary surgeon. Finally, when sciatica exists without obvious cause and medical treatment proves ineffectual, the nerve should be exposed by an incision and examined for adhesions. The operation entails but little risk and offers a very considerable chance of permanent relief. Nerve stretching occasionally does good, but in the large majority of cases it fails.

**Anterior Metatarsalgia (Morton's Disease).**—This term is applied to a painful affection caused by pressure upon the digital branches of the external plantar nerve. The pain, which is excited by walking or standing, is usually located at the base of the fourth toe and is increased by pressure with the finger over the head of the fourth metatarsal bone. However, pain of similar origin is not uncommon at the distal ends of the other metatarsal bones. The exciting causes are, as a rule, the use of ill-fitting shoes (narrow toes) and depression of the anterior arch, or of this arch and the longitudinal arch (flatfoot). Calluses or corns under the depressed heads of the bones or neuritis from other causes than pressure may also be responsible for the condition. Relief is often afforded by wearing a well-fitting shoe with a broad sole, high arch and low heel, strapping adhesive plaster over the metatarsus, and inserting a pad under the affected joint or under the whole anterior arch. If there is flatfoot a metal brace should be used that will support both the anterior and longitudinal arches. After the pain has been relieved, massage and passive movements are beneficial. Refractory cases demand surgical intervention—excision of the superficial branch of the external plantar nerve, amputation of the fourth toe, or transplantation of the long extensor tendon into the head of the affected metatarsal bone (A. M. Forbes).

## NEURALGIA

**Definition.**—The term neuralgia is used to denote pain occurring paroxysmally along the peripheral ramifications of a nerve and caused by pathogenic irritation affecting the nerve at some point or other of its course. Anatomically, it is difficult to establish a sharp distinction between neuralgia and neuritis, although clinically the two conditions have little in common. Neuralgia is always a symptom, but the fundamental condition of which it is a manifestation is by no means definitely known. The fifth cerebral (trigeminal) nerve is the one affected in the large majority of cases, but

[1] For details see article by Strauss, Jour. Amer. Med. Assoc., Dec. 15, 1917.
[2] Minnesota Med., Dec. 12, 1921.

occasionally other nerves, such as the cervico-occipital, intercostal, cervico-brachial and sciatic, are involved.

## TRIGEMINAL NEURALGIA

(Trifacial Neuralgia; Tic Douloureux)

**Etiology.**—Trigeminal neuralgia occurs most frequently between the ages of 30 and 50 years. It is rare in childhood and old age. Women are more subject to the disease than men. Examples of direct hereditary transmission are exceptional, but a history of migraine, epilepsy, hysteria or some other neurosis in the ancestry is often obtainable. Acute infections, particularly influenza, are responsible for a certain number of cases. Herpes zoster, which must be included among the infectious processes, sometimes results in a refractory form of neuralgic pain—"postzoster neuralgia." The most severe cases are those affecting the ophthalmic division of the fifth nerve. Syphilis is an occasional etiologic factor, and so is malaria, but it should be borne in mind that the regular recurrence of the painful paroxysms and a history of intermittent fever do not in themselves establish the identity of malarial neuralgia. Certain disorders of nutrition, such as pronounced anemia, and certain chronic intoxications, such as diabetes, gout, lead-poisoning, and alcoholism, seem to favor the occurrence of the disease. Influences that exhaust the nervous system, such as overwork and prolonged lactation, may also act as predisposing factors. Irritation of the nerve arising from dental caries, an impacted tooth, or inflammation of the accessory nasal sinuses not rarely results in a neuralgic condition. Traumatism is an occasional factor. Tumors that arise from structures adjacent to the Gasserian ganglion and involve it by direct pressure or that arise from the capsule of the ganglion itself (endotheliomas) are capable of producing neuralgic pain. Finally, in a very large proportion of cases it is impossible to find any adequate cause for the painful paroxysms.

Exposure to cold, a sudden atmospheric change, mental excitement, fatigue or even slight irritation in the trigeminal field, such as occurs in eating, talking, yawning, brushing the teeth, or washing the face, is often sufficient to excite an attack of pain when the affection already exists.

**Pathology.**—Nothing certain has yet been discovered as to the anatomic foundation of trigeminal neuralgia. Some believe that the disease is due to changes in the cells of the Gasserian ganglion, but there is not much evidence to support this view.

**Symptoms.**—Pain referred to the parts traversed by any one or all of the divisions of the trigeminal nerve is the chief symptom. The pain occurs in paroxyms, repeated at intervals usually of a few seconds' or minutes' duration, and is often intolerably violent. The character of the pain varies, but, as a rule, it is described as piercing, cutting, tearing or burning. A series of successive paroxsyms constitutes an attack. The latter may pass away in a few minutes or it may last several hours or days. Following it there is an interval of complete relief, which varies in duration from a few days to many weeks. Usually as the disease progresses the attacks increase both in frequency and severity.

During the attacks, and sometimes between them, points of extreme tenderness —the *puncta dolorosa* of Valleix—are found in the course of the nerve where the affected branches emerge from bony canals or pierce fasciæ and become superficial. When the first or ophthalmic division of the fifth nerve is involved the pain is felt above the eye as far as the vertex, in the eyelid, in the eye itself, and at the side of nose, and tender points are found at

the supraorbital notch, at the lower margin of the nasal bone, and sometimes in the outer part of the upper eyelid. When the second or superior maxillary division is affected the pain radiates between the eye and the mouth and at times into the teeth and gums of the upper jaw; the chief tender focus is at the infraorbital foramen. In neuralgia of the third or inferior maxillary division the pain is referred to the ear, cheek, lower jaw and tongue; the principal tender points are in front of the tragus, over the parietal eminence, at the mental foramen and in the tongue.

The pain may never extend beyond the territory of one branch of the nerve, but in many cases it tends sooner or later to spread into the regions supplied by the other divisions, and, occasionally it overflows to the neck, shoulder and even the arm. Frequently, irritation in the distribution of one of the three branches will induce pain in another branch. In exceptional cases trigeminal neuralgia is bilateral.

Associated with the sensory disturbances there may be certain vasomotor, secretory, motor and trophic disorders. The most common vasomotor disturbance is flushing and slight swelling of the skin in the area of pain. The secretory disorders usually consist of an abnormal flow of tears or saliva and local sweating. The chief motor phenomenon is the occurrence of forcible chewing movements from excitation of the masticatory muscles. Trophic anomalies are uncommon, but occasionally whitening of the hair and thickening of the skin eventually occur in the region of the affected nerve.

While the intervals separating the attacks may be entirely devoid of symptoms, it is not uncommon to find diffuse hyperesthesia of the skin in the involved area, as well as the "tender points" to which attention has already been drawn.

**Diagnosis.**—This is usually easy. Other neuralgic conditions involving the face, such as painful spasmodic tic, pain from irritation of the sensory division of the seventh nerve (Hunt's neuralgia), pain from involvement of Meckel's ganglion (Sluder's neuralgia), and pain from involvement of the trigeminus by tumors, as well as ordinary migraine, must be excluded.

*Painful tic convulsif* is distinguished by the characteristic contracture of the face, which bears little resemblance to the facial contortions and masticatory movements of true trigeminal neuralgia. In *neuralgia of the sensory division of the seventh nerve* (*Hunt's geniculate neuralgia*) the pain is especially marked in front of the ear, although it may begin in the throat or palatal region, and accompanying the pain there is usually facial palsy or herpes within the auditory meatus. In Sluder's[1] neuralgia, which is comparatively rare, there is evidence of sinus disease and the pain is frequently bilateral, is more or less persistent, is not excited by slight peripheral irritations about the face, and shows a greater tendency to radiate to the neck and shoulder than that of true *trigeminal neuralgia*. *Tumors with facial neuralgia* may usually be recognized by the persistent character of the pain, the general pressure disturbances, and the involvement of other cranial nerves, and not rarely by an accompanying hypesthesia and motor-fifth paralysis.

In *migraine* the pain is not inaugurated by slight peripheral irritations about the face, it is more continuous and more diffuse than that of neuralgia, and it does not definitely correspond to the distribution of the trigeminus; "tender points" are absent, visual disturbances are commonly noted at the onset of the attack; and vomiting usually occurs at the height of the pain. It must not be foregotten, however, that trigeminal neuralgia occasionally develops on the basis of a migrainous neurosis. The serious error of mistaking *acute glaucoma* for supraorbital neuralgia has sometimes been made.

[1] Sluder, G.: Headaches and Eye Disorders of Nasal Origin, St. Louis, 1918.

**Prognosis.**—The prognosis must be guarded, especially if the disease is of long duration and the cause is not manifest or, if manifest, is one that cannot be removed. Of the severe trigeminal neuralgias, the majority are only amenable to operative treatment, and even this is not invariably successful.

**Treatment.**—An effort should be made to adapt the treatment to the etiology of the disease. Causes of peripheral irritation, such as dental caries, inpacted teeth, inflammation of the accessory nasal sinuses, etc. should be sought, and when found removed, if possible. If the disease is associated with marked anemia iron and arsenic are indicated. If there is evidence of syphilis arsphenamin, mercury and iodids should be tried. If a malarial element is present quinin may effect a cure. All influences that tend to induce morbid irritability of the nervous system, such as mental or physical fatigue, undue emotional excitement, sexual excesses, and over-indulgence in tea, coffee, alcohol and tobacco, should be eliminated, if possible. An effort should be made also to improve the general nutrition, which in many cases is much impaired. For this purpose an abundance of fresh air, appropriate food, regular hours, adequate protection from vicissitudes of weather, systematic exercise, frequent bathing with friction of the skin, and tonic remedies are requisite. Neuralgia in neurasthenic patients is sometimes successfully managed by the Weir Mitchell treatment or a modified form of it. A change of residence to a warm dry climate is often helpful.

Many special remedies have been recommended, but few are worthy of confidence. Dana and others speak favorably of strychnin in heroic doses in *tic douloureux* occurring in anemic and exhausted patients and when the duration of the disease does not exceed one or two years. The drug is given hypodermically once a day and the dose is gradually increased from $\frac{1}{30}$ grain (0.002 gm.) to $\frac{1}{15}$ grain (0.13 gm.), 10 to 12 days being required to reach this maximum. During the treatment the patient should be kept in bed and closely observed.

For the attack itself the coal-tar analgesics (acetphenetidin, antipyrin and acetanilid) are the most generally useful remedies. From 5 to 8 grains (0.3–0.5 gm.) may be given every two to four hours, according to the intensity of the pain. It must be borne in mind, however, that these agents when used repeatedly not only lose their potency, but also unfavorably affect the patient's general nutrition. Injections of morphin are undoubtedly the most certain means at our command of affording temporary relief, but on account of the great danger of inducing a habit, this measure should be employed only as a last resort. Combinations of a bromid or of caffein with acetphenetidin or antipyrin are sometimes more effective than the coal-tar analgesics alone. Aconitin ($\frac{1}{400}$ grain—0.00016 gm.), tincture of gelsemium (10–15 min.—0.6–1.0 mil), and butyl-chloral hydrate (5–10 grains—0.3–0.6 gm.) are occasionally servicable. Neuralgic attacks that are excited by exposure to cold are often favorably influenced by salicylates in large doses.

*Local Treatment.*—Heat, dry or moist, may be applied for its soothing effect. Occasionally cold applications are more agreeable. Menthol or choral-camphor is useful in mild attacks. A spray of ethyl chlorid is sometimes efficacious, especially in post-zoster neuralgias. In using it about the face, however, the eyes must be carefully protected. Electricity in the form of a mild continuous galvanic current has its advocates. In refractory cases the application of a blister back of the ear is sometimes of benefit.

In the majority of cases the attacks eventually become so severe and the remissions so short that recourse must be had to operative treatment, especially alcoholic injection, peripheral neurectomy or avulsion of the

sensory root of the Gasserian ganglion. Treatment by injection of alcohol (80–90 per cent.) into the nerves near their foramina of exit from the skull, which was introduced by Schlösser[1] in 1903, may be recommended when the pain is limited to one of the two lower divisions of the nerve and even when all three divisions are affected if the patient's condition is such as to unfit him for the more radical Gasserian operation. Moreover, as Cushing[2] has pointed out, it is sometimes useful in determining in doubtful cases whether the syndrome is a true neuralgia of the tic douloureux type or one of the peculiar and rare pseudoneuralgias not amenable to relief either by injections or neurectomies. Alcohol injection does not result in a permanent cure, but it usually gives complete relief for an average period of from eight months to a year. It has almost entirely superseded peripheral neurectomy, except in the case of supraorbital neuralgias, in which it has not been very effective. Post-zoster neuralgia should not be treated by alcohol injection or by any other operative measure. The injection treatment is safe when properly practiced, but in the hands of the inexperienced it is not uncommonly followed by secondary hemorrhage, oculomotor palsy, facial paralysis, stiff jaw, secondary keratitis or labyrinthine vertigo. The injection of alcohol directly into the ganglion itself has been done with some success, but it seems more likely to result in complications than the radical operation of removing the sensory root. The radical operation almost always affords permanent relief from the pain, although it results in localized anesthesia. In skillful hands the risk is small. Cushing[3] reports 332 operations with 2 deaths in the first 34 and none in the last 298, and Frazier[4] reports a series of 157 consecutive operations with 1 death (0.6 per cent.)

## OTHER FORMS OF NEURALGIA

**Cervico-occipital Neuralgia.**—Neuralgic pain in the course of the upper four cervical nerves may result from any of the causes of neuralgia elsewhere. It is usually due, however, to arthritis of the cervical spine, cervical adenitis, chronic pachymeningitis, or traumatic lesions of the plexus. Occasionally, it is associated with trigeminal neuralgia. The pain, which is chiefly felt in the occipital region, may be unilateral or bilateral. Movements of the head increase it and therefore "stiff neck" is not an uncommon accompaniment. Tender points may be found at the exit of the great occipital nerve (the branch most often affected) between the mastoid process and the spine, between the sternomastoid and trapezius muscles, and near the parietal protuberance. Between the paroxysms the scalp in the affected area is frequently hyperesthetic.

**Intercostal Neuralgia.**—Intercostal neuralgia shares in the general etiology of other neuralgias. It is often associated with herpes zoster. As a rule, the eruption does not develop until the pain has lasted for several days, but sometimes, particularly in old persons, the eruption is first to appear. Persistent or frequently recurring pain in the intercostal spaces is almost always the result of organic disease, such as thoracic aneurysm, chronic inflammation in the vertebræ, or spinal tumor. So-called idiopathic intercostal neuralgia is very rare.

The pain, which is usually unilateral, is referred definitely to the course of the dorsal nerves. Occasionally it radiates to the arm. Deep breathing

[1] Nerven. Ztschr. f. Augenh., 1903, x, 335.
[2] Jour. Amer. Med. Assoc., Aug. 14, 1920.
[3] Amer. Jour. Med. Sci., Aug., 1920.
[4] Jour. Amer. Med. Assoc., Jan. 8, 1921.

and coughing, as a rule, intensify it. Points of tenderness are usually found near the spine, in the midaxilla or at the edge of the sternum. In *myalgia* (pleurodynia) the pain is more diffuse and less sharply limited to the area of distribution of the nerves, and the characteristic tender points are wanting. *Angina pectoris* is readily distinguishable by the ensemble of symptoms accompanying the pain.

**Mammary Neuralgia.**—This rare form of intercostal neuralgia is met with in women and usually makes its appearance during menstruation, pregnancy or lactation. The pain is deep seated and is frequently associated with pronounced hyperesthesia of the skin, especially about the nipple.

**Cervicobrachial Neuralgia.**—Pain in the shoulder and arm, in the area of distribution of the four lower cervical nerves and the first thoracic nerves (brachial plexus), is only in very rare instances the expression of a simple neurosis. In the vast majority of cases it depends upon organic disease in some structure with which the affected nerves are in anatomic relation or is an indication of actual neuritis. It may be caused by enlarged lymph-nodes, deposits of callus, caries of the vertebræ, arthritis of the spine, or shoulder joint, tumor of the spinal cord or of its membranes, hypertrophic cervical pachymengitis, traumatic lesions, chronic fibrositis, bursitis, a supernumerary cervical rib, etc. In some cases of angina pectoris the pain is felt in the arm only. Finally, pain in the shoulder or arm may be a symptom of uncomplicated neuritis resulting from a general infection, overuse of the muscles, etc.

**Sciatic Neuralgia.**—Pain referred to the course of the sciatic nerve is usually termed sciatica. In the large majority of cases such pain is a symptom of organic disease in some structure with which the sciatic nerve is in anatomic relation, such as the lower spine, the lumbosacral, sacroiliac, or hip joint, the cauda equina, or the pelvic viscera, especially the prostate gland (see p. 930). Occasionally, sciatica is the expression of an actual neuritis resulting from some infection or intoxication (diabetes, gout). True sciatic neuralgia is extremely rare.

## HERPES ZOSTER

**(Zona; Shingles[1])**

Herpes zoster is an acute inflammatory disease affecting the posterior spinal ganglia, the Gasserian ganglion or other sensory ganglia, and characterized by neuralgic pains and the development of groups of vesicles upon inflammatory bases in the skin zone corresponding to the diseased ganglia. Symptomatic and primary forms are recognized.

**Symptomatic herpes zoster** occurs in the course of other conditions incidentally affecting the sensory ganglia. Thus, it may be observed in certain nervous diseases, such as meningitis, tabes dorsalis and general paresis; in various specific fevers, such as varicella, influenza, pneumonia and malaria; in certain intoxications, particularly that due to arsenic; and in lesions of the vertebræ involving the ganglia, such as tuberculosis, carcinoma, spinal injuries, etc.

**Primary herpes zoster** is an acute infectious disease, probably due to a specific agent having an affinity for the sensory ganglia. The studies of Rosenow and Oftedal[2] suggest that a streptococcus is the cause.

[1] Lat., *Cingulum*, a girdle.
[2] Jour. of Infect. Diseases, May, 1916.

**Etiology.**—The disease may occur at any age. Exposure to cold and debility from various causes seem to favor its development. Occasionally it has been epidemic. A second attack is rare.

**Morbid Anatomy.**—The inflammatory process affects chiefly one sensory ganglion, although the adjacent ganglia may be involved to a slight extent. The lesions consist of marked congestion, hemorrhages, round-cell infiltration and foci of degeneration. Retrograde changes may occur also in both the peripheral and central portions of the posterior roots and occasionally in the posterior horns of the spinal cord (Hedinger). The cutaneous vesicles are probably secondary trophic effects, for in the early stages they do not contain organisms.

**Symptoms.**—Neuralgic pain, often severe, usually precedes the attack by a few days or appears synchronously with it, and not rarely other prodromal symptoms, such as chilliness, malaise, slight fever, and gastrointestinal disturbances, are also noted. In some instances, particularly in childhood, pain is slight or entirely absent. The eruption, which is almost always unilateral, appears most frequently on the chest, but it is not uncommon on the face, head, neck and extremities, and occasionally it is seen on the mucous membrane of the pharynx and larynx. It consists of irregular groups of pinhead to pea-sized vesicles resting on inflammatory bases. The distribution of the lesions does not follow closely the course of the peripheral nerves, as is usually stated, but is segmental and corresponds to the ganglia and roots affected. In from a few days to two weeks the vesicles dry and form yellowish-brown crusts, which eventually drop off leaving, as a rule, no trace, but occasionally considerable scarring. In some cases, owing to secondary infection, the lesions become pustular and even gangrenous. In addition to the neuralgic pain, burning and itching are often experienced at the site of the vesicles.

Ophthalmic zoster, which is most frequently seen in feeble elderly persons, sometimes results in destructive inflammation of the cornea, iris, and indeed of the whole eye. Paralysis of the oculomotor nerve, atrophy of the optic nerve and glaucoma have also been observed. Facial and aural zoster may give rise to various auditory disturbances and to paralysis of the facial nerve (Bell's palsy). The latter may come on at the time of the eruption or several days later.

In some instances, particularly of ophthalmic zoster, severe and intractable neuralgia remains for years after the subsidence of the eruption.

**Diagnosis.**—This, after the appearance of the eruption, presents no difficulties. Pre-zonal neuralgia, however, may readily be misinterpreted. Occurring in the chest it may suggest pleurisy, over the liver, gall-stones, and in the ear, otitis media.

**Treatment.**—Locally, a dusting powder of zinc oxide (8 parts), boric acid (8 parts), talc (8 parts) and camphor (1 part), or zinc ointment containing 5 gr. (0.3 gm.) of menthol to the ounce (30.0 gm.) may be used and the parts covered with a layer of cotton. In outbreaks near the eye, the conjunctiva should be frequently washed with a solution of boric acid. For the relief of pain phenacetin, salicylates, bromids and codein may be given. The following combination is often useful:

℞. Codeinæ sulphatis..... gr. iss–ii (0.1–0.13 gm.)
Acetphenetidini.....
Acidi acetylsalicylici..... gr. āā xl (2.65 gm.) M.
Ft. chart. No. xii.
Sig.—One every three hours.

For protracted cases zinc phosphid, quinin and strychnin, and a mild galvanic current have been recommended.

### GENERALIZED NEUROFIBROMATOSIS

(Von Recklinghausen's Disease)

Generalized neurofibromatosis is a rare disease characterized by the occurrence of fibroma of the skin in multiple form. It is often hereditary, sometimes familial, and probably always congenital, although the lesions may become conspicuous only in later life. Its symptoms have many points of contact with those of adiposis dolorosa, and it is not improbable that some disturbance of the glands of internal secretion is concerned in both processes.

**Morbid Anatomy.**—As von Recklinghausen[1] pointed out, the tumors arise from the sheaths of the cutaneous nerves and are composed chiefly of fibrous tissue, although a few nerve fibers may run through them. In some instances the internal organs are affected as well as the skin, and occasionally gliomata are present in the central nervous system.

**Symptoms.**—The chief feature is the appearance on the surface of the body of numerous sessile or pedunculated, soft or firm, nodules, varying in size from that of a millet seed to that of an orange. Pigmentation of the skin over the nodules or elsewhere is frequently noted and nevus formations, both capillary and cavernous, are also common. Subjective disturbances may be absent, but tenderness at the site of the lesions and neuralgic pains are not infrequent. Feeble-mindedness or an actual psychosis is often present and neurasthenic symptoms sometimes supervene. Scoliosis and other skeletal deformities have been observed in a number of instances. The association of the disease with acromegaly has been mentioned by Thomas, De Castro, Wolfsohn and Marcus, Cushing and others. The tumors are usually benign, but in some families they tend to develop into sarcoma (Preiser and Davenport[2]).

**Treatment.**—Growths that cause inconvenience may be removed by excision, the galvanocautery, or electrolysis. In a case cited by Whitehouse[3] the nodules disappeared under the long-continued use of arsenic.

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## DIFFUSE AND FOCAL DISEASES OF THE BRAIN

### CEREBRAL APOPLEXY

The word apoplexy, which literally means a "stroke," was for a long time used as a synonym for cerebral hemorrhage. Later, its use was extended to effusions of blood occurring suddenly into other organs or tissues, as the lungs, suprarenal capsules, and retinæ. At present, in its application to the brain, the term is generally employed to designate a sudden disturbance of the cerebral function, arising either from hemorrhage into brain or from the occlusion of a cerebral bloodvessel by an embolus or thrombus, these two conditions producing symptoms so nearly alike that it is often impossible to distinguish between them.

[1] Ueber die multiplen Fibrome der Haut und ihre Bieziehung zu den multiplen Neuromen, Berlin, 1882.

[2] Amer. Jour. Med. Sci., Oct., 1918.

[3] Jour. Cutan. Dis., 1899.

## CEREBRAL HEMORRHAGE

**Etiology.**—Intracranial hemorrhage that is not of traumatic origin is almost invariably dependent upon changes of a degenerative or inflammatory character in the smaller cerebral bloodvessels. In many cases the miliary aneurysms first described by Charcot and Bouchard[1] in 1868 are the vascular alterations immediately responsible for the extravasation. However, these sacculations, which usually measure about ½–1 mm. in diameter, depend upon arteriosclerosis and frequently represent circumscribed hemorrhages into the sheaths of the arteries (dissecting aneurysms) or into the circumvascular lymphatic spaces (false dissecting aneurysms) rather than true aneurysmal dilatations (Benda, Pick, Ellis). Not rarely the vessels are more uniformly affected and the rupture occurs without previous aneurysm formation.

The predisposing causes of cerebral hemorrhage are those that favor the occurrence of arterial disease. Age is an important factor. Although no period of life is exempt, the period between 40 and 60 is the one in which the large majority of cases occur. Men owing to their greater tendency to arterial disease are more frequently affected than women. Heredity is not without influence, a disposition to arteriosclerosis being especially marked in certain families. The so-called *habitus apoplecticus*—a stocky body with a short thick neck—does not seem to play any considerable rôle. Syphilis, gout, alcoholism, chronic renal disease and prolonged muscular strain must be included among the etiologic factors, because of their influence in hastening vascular decay.

Arteriosclerosis is particularly dangerous when associated with persistent hypertension; for while a diseased artery may burst when it is under a pressure that is normal or only relatively high it is much more likely to do so when subjected to a pressure that is absolutely increased. Hence, the combination of arteriosclerosis with hyperpiesis, which so frequently obtains in chronic glomerulonephritis is especially favorable to hemorrhagic apoplexy.

Occasionally, vessels of the brain rupture in consequence of morbid changes that have been produced in their walls by acute infectious diseases, such as diphtheria, scarlatina or whooping cough, or by profound alterations in the blood, as in pernicious anemia, purpura hemorrhagica, etc. Finally, cerebral hemorrhage may result from the breaking down of a vascular tumor of the brain or from the opening of an abscess into a bloodvessel of the brain. The attack usually occurs without any obvious exciting cause. It may be precipitated, however, by excessive muscular exertion, great mental excitement, over-eating, or alcoholic intoxication; it may be brought on by coitus, or it may follow a blow upon the head, immediately, or, as in cases cited by Bruns, Stadelmann, Marie[2] and others, after an interval varying from a few days to several weeks.

**Morbid Anatomy.**—The hemorrhage may be meningeal or intracerebral.

*Meningeal Hemorrhages.*—These may occur on the outer or inner surface of the dura or between the pia and arachnoid. Large effusions are usually due to traumatism. Less frequently they result from the rupture of an aneurysm or of a large vascular tuft in chronic internal pachymeningitis (see p. 895). Small punctate hemorrhages not rarely occur in the specific fevers, hemorrhagic diseases, acute meningo-encephalitis, and asphyxia. Meningeal hemorrhages in the new-born are usually due to trauma at birth.

[1] Arch. de Physiol. normal et Pathol, 1868.
[2] Revue de Méd., May 10, 1905.

*Intracerebral Hemorrhages.*—These may involve any portion of the brain. The most frequent site is the region in the neighborhood of the internal capsule, which is supplied by the lenticulo-striate and lenticulo-thalamic branches of the middle cerebral artery. The first of these vessels is so especially liable to disease and rupture that it has been termed the "artery of cerebral hemorrhage" (Charcot). Both vessels lack collateral branches and are subjected to a high pressure, and it is probably for these reasons that about two-thirds of all intracranial hemorrhages result from their rupture. In many cases the hemorrhagic effusion does not extend beyond the boundaries of the basal ganglia and the internal capsule; somewhat frequently, however, it works its way inward and bursts into the lateral ventricle, and in exceptionally severe cases it may destroy almost the whole of one hemisphere. Hemorrhages in parts of the brain other than the basal ganglia occur in about the following order: centrum ovale, convolutions of the cerebrum, pons and cerebellum. Hemorrhages into the crura, corpus callosum, and medulla are infrequent. Primary ventricular hemorrhage occasionally occurs from rupture of a vessel of the choroid plexus or velum interpositum.

The appearances presented by hemorrhage into the brain vary with the time that has elapsed since its occurrence. In recent cases the extravasated, blood is dark in color, clotted, and often intermingled with fragments of nerve-tissue. If the patient survives the clot shrinks and becomes much paler, blood-pigment is set free and stains the adjacent tissue, and soon an inflammatory reaction ensues at the periphery of the lesion, leading to the formation of a fibrous capsule. In the course of time the coagulum itself may be entirely absorbed, leaving only a more or less pigmented cicatrix, or after the site of the hemorrhage has been cleared of softened tissue by absorption, it may be occupied by a cyst containing clear or slightly bloody serum.

Finally, as a result of the destruction of brain-tissue, the important change known as secondary degeneration occurs and proceeds in the direction in which the nerve-fibers convey impulses. The extent of this process depends, of course, upon the amount of nerve-tissue destroyed. After complete division of the internal capsule, a path of degeneration may be traced from the site of the lesion through the crus, the pons, the medulla, the crossed pyramidal tract on the opposite side of the cord and the direct pyramidal tract on the same side.

**Symptoms.** *Prodromes.*—Certain symptoms arising from disturbance of the cerebral circulation are frequently experienced by the patient for several days, weeks, or even months before the occurrence of the actual seizure, though they are much less common with hemorrhage than with thrombosis and softening. These premonitions usually consist of dull headache, vertigo, irritability, insomnia, and tinnitus aurium. Sometimes attacks of nose-bleed occur, and exceptionally there are sensations of numbness, tingling or heat, neuralgic pains, muscular cramps or even choreiform movements in the extremities of the one side. Just before the "stroke" there may be marked restlessness, awkwardness of movement, mental confusion, disorientation or vomiting.

*The Attack.*—In many cases, however, prodromes are entirely absent and the patient is stricken in the midst of apparently good health. The symptoms of the attack vary with the location and extent of the hemorrhage. Ordinarily loss of consciousness and paralysis of one side of the body are the conspicuous features. The patient, if standing or sitting, generally falls, deprived of consciousness at once (fulminant apoplexy) or losing it gradually in a few minutes or, possibly, in a few hours. The *coma*, when fully developed, is usually attended by congestion of the face, loud stertorous breathing, an

infrequent, full, strong pulse, general muscular relaxation and a loss of the tendon reflexes. Owing to the increased intracranial tension the blood-pressure is usually high. The *pupils* are variable. Frequently, they are dilated, but sometimes, especially in lesions of the pons, they are contracted. In either case they are usually sluggish or immobile. Not rarely they are unequal. The *temperature* during the first three or four hours may be normal or subnormal; later, except in rapidly fatal cases, it is usually somewhat elevated (100°–102°), being about a degree higher on the paralysed side than on the sound side. The *urine* in some instances is passed involuntarily; in others it is retained. Not rarely, it contains traces of albumin or sugar. If there is enough of the internal capsule remaining to convey motor impulses *convulsions* may occur, but they are not common. When confined to the paralyzed side they strongly suggest a cortical lesion.

Even during the continuance of the coma the *paralysis* usually declares itself in a number of ways. Thus, it may be noted that one cheek is more puffed out during expiration than the other; that one corner of the mouth droops; that the extremities of one side when raised drop more limply than those of the opposite side, or, less frequently, that the members of one side (paralyzed side) are rigid, while those of the other side are relaxed; and that instinctive movements are absent on one side and not on the other. Another frequent indication of hemiplegia, and one of unfavorable significance, is so-called *conjugate deviation* of the eyes and head. This consists in a forcible deflection of the eyes and head to one side.

Occasionally, the eyes alone are involved. In lesions above the pons, the patient looks away from the palsied side; whereas in lesions of the pons or below the pons, he looks toward the palsied side. During convulsions, however, the direction of the deviation is usually reversed. In some instances instead of complete deviation there are jerking or nystagmoid movements of the eyes in a lateral direction. Choked disc is sometimes found on ophthalmoscopic examination (Uhthoff[1]).

An attack that proves fatal usually lasts from a few hours to several days. Sudden death within a few minutes is rarely, if ever, observed. As the end approaches the pulse becomes frequent and feeble, the respiration grows irregular or assumes the Cheyne-Stokes type, the face turns pale, the sphincters relax, the temperature falls or, contrariwise, rises to a considerable height, and mucus collects in the trachea, producing the so-called "death rattle." Not rarely when the patient survives for twenty-four hours and the coma continues, or even, in some instances, when there has been a restoration of consciousness, a reaction occurs, which is the outcome of inflammation around the clot. This phase of the attack is marked by restlessness, more or less febrile disturbance, and, in case consciousness has been regained, by delirium or, perhaps, a return of coma. Sometimes too the muscles of the affected limbs, heretofore relaxed, become rigid (*early rigidity*) and occasionally sloughing occurs over the sacrum or over the buttock of the palsied side. In the course of a few days or weeks pneumonia may supervene and hasten the end. In other cases the reaction is very slight and does not appreciably interfere with recovery.

While cerebral hemorrhage is usually fatal, it is not invariably so. In some cases the patient after remaining in a comatose or stuporous state for several hours or a day, rarely longer, recovers his mental faculties and shows signs of improvement in his general condition. The paralysis also may gradually decrease and at the end of a few weeks no evidence of the attack may remain. But such an entirely favorable outcome is exceptional.

[1] Neurolog. Centralbl., 1909, No. 20.

Much more frequently with the subsidence of the acute symptoms, the patient enters upon a chronic stage of the disease still suffering from more or less complete hemiplegia and, perhaps, also from aphasia.

Of course, the phenomena of the attack are liable to many variations. Instead of the flushed face, bounding pulse, and noisy respiration, there may be pallid features, a feeble pulse, and quiet breathing. In some cases the onset is sudden with headache, vertigo, and perhaps vomiting, but without loss of consciousness; the paralysis develops more or less rapidly, and later, after the lapse of several hours, somnolence sets in and deepens into coma (*ingravescent apoplexy*). In other instances the appearance of paralysis is attended by transient mental confusion, vertigo, or feeling of faintness, but consciousness is not actually lost at any time. In exceptional cases aphasia and hemiplegia are the first and only symptoms. Sometimes the attack occurs during sleep and the first intimation that there is anything wrong is the discovery by the patient that an arm and leg are limp and powerless when he attempts to rise from his bed in the morning.

In meningeal hemorrhage severe headache, vomiting, and myosis, followed by rigidity and muscular twitchings on one side, or in their stead, hemiparesis, gradually increasing in degree, may be the symptoms produced. Hemorrhages into the frontal lobes, unless they extend backward to the motor area or break into a lateral ventricle, often cause little or no paralysis.

Pontile hemorrhages are frequently characterized by profound coma, high temperature (104°–108°) pin-point contraction of the pupils, muscular twitchings, and single or double hemiplegia, with paralysis of the fifth, sixth or seventh nerves. If the lesion be in the lower part of the pons there may be hemiplegia on the opposite side and facial paralysis on the same side (crossed paralysis).

In cerebellar apoplexy there may be no localizing symptoms, but merely coma, stertorous breathing, myosis, and general muscular relaxation.

*Chronic Stage.*—The paralysis remaining after an apoplectic attack is commonly *hemiplegia* or *hemiparesis*, the side opposite the cerebral lesion being affected. The corner of the mouth on the paralyzed side droops and that on the sound side is drawn upward. Although the patient is unable to inflate the cheek or whistle, he can usually wrinkle the forehead and move the eyelids, probably because the muscles of these parts being accustomed to act in unison receive a bilateral cortical innervation. The facial palsy is much less apparent in emotional expression, as in smiling and weeping, than it is in voluntary efforts, which fact may also be explained on Broadbent's hypothesis that muscles used involuntarily are innervated from both cerebral hemispheres. The tongue is also involved. When protruded it deviates toward the paralyzed side, owing to the predominance of the sound genio-hyo-glossus muscle. This lingual disability, even more than the facial paresis, is responsible for the thickness of speech that is frequently observed in hemiplegics.

The limbs present varying degrees of paralysis from slight weakness to complete immobility. As a rule, the arm is more affected than the leg and the distal portion of the extremity more than the proximal portion. Except very early in the attack, the *tendon reflexes* on the paralyzed side are exaggerated. Ankle clonus may often be elicited and Babinski's sign (dorsal extension of the great toe upon stroking the outer margin or ball of the foot with a blunt-pointed instrument) may almost invariably be obtained. On the other hand, the cremasteric, abdominal and other *cutaneous reflexes* are almost always absent. Although the respiratory movements are represented bilaterally in the brain, they are peculiarly affected. During quiet breathing

they are greater on the paralyzed side, but during forced or volitional breathing they are greater on the sound side (Jackson, Clarke, Bury, Weisenberg[1]).

The *gait* of the hemiplegic is characteristic. The paralyzed leg is carried forward by a movement of circumduction proceeding largely from the trunk, the toe often dragging as it goes along.

In from 2 or 3 weeks to 2 or 3 months, if the paralysis persists, the affected muscles pass into a state of contraction, which is known as "*late rigidity.*" This condition, always more marked in the arm than in the leg, is supposed to be a result of secondary degeneration in the pyramidal tract. It usually fixes the arm in a position of flexion and the leg in a position of extension. In some cases an admixture of spasticity and flaccidy is found in the same limb, and in rare instances, as a result of complete destruction of the internal capsule and pyramidal tract, the paralysis remains flaccid or toneless indefinitely.

Sometimes, although very rarely in adults, the paralyzed parts become the seat of certain *involuntary movements.* These may take the form of chorea (post-hemiplegic chorea), athetosis, or tremor. Occasionally, "associated movements" are noted. These occur on the paralyzed side synchronously with voluntary movements on the sound side. *Aphasia* is a frequent accompaniment of right hemiplegia. Exceptionally, it is the only symptom of the disease.

*Hemianesthesia* is present in some cases of apoplexy, but, as a rule, it is partial and transitory. *Paresthesia,* muscular soreness and even neuralgic pains are not uncommon. Impairment of the *muscular sense* and of the *stereognostic sense* (perception of form and of physical properties of objects by means of touch) is not infrequently observed. Hemianopsia may also be noted.

Although the paralyzed muscles usually remain well nourished for a long time, they occasionally exhibit after the lapse of several months more or less *atrophy.* It is surmised that this muscular wasting is due to the suppression of certain trophic influences that the cortical neurons have over those of the spinal cord. In some instances, at least, it is too pronounced to be ascribed to inactivity alone. With the lapse of time the skin of the affected limbs becomes somewhat cooler than normal and often takes on a cyanotic hue. Slight *edema* may also develop. Mills found it in 7 of 60 cases. Whether it is due to venous stasis from muscular inactivity or to vasomotor paresis is not clear. *Joint changes* occasionally occur. These may be of inflammatory type or of a degenerative nature. Finally, a certain proportion of hemiplegics suffer from more or less *mental impairment.* This is usually manifested by weakness of memory and loss of emotional control, but in some cases actual dementia ensues.

**Diagnosis.**—The diagnosis of cerebral hemorrhage is often very difficult, especially when the previous history of the patient is not known. Although the signs of unilateral paralysis are always of the greatest significance, it must be remembered that these may also be produced by embolism and thrombosis of the cerebral arteries—conditions which cannot always be excluded with certainty (see p. 947), and, on the other hand, that in cases of severe hemorrhage the general muscular relaxation may be so marked that palsy of one side cannot readily be detected. The diagnosis of hemorrhagic apoplexy is usually justified, however, when hemiplegia is manifest and is associated with congestion of the face, a full bounding pulse, noisy respiration, and elevation of temperature.

[1] This phenomenon is usually ascribed to a loss of cortical inhibitory control over the respiratory center as a result of which the center overacts in automatic breathing.

Chief among the conditions capable of producing more or less sudden coma and therefore likely to be mistaken for cerebral hemorrhage are skull fracture, opium poisoning, alcoholic intoxication, uremia, diabetic acidosis, epilepsy and sunstroke. *Skull fracture* may be difficult to exclude, especially when there is little evidence of external injury. Commonly, however, the history of an injury will be obtainable, and, with a fracture at the base, blood may be seen coming from the ear or nose or ecchymosis may be found beneath the conjunctiva, around the eye, or about the mastoid process. Bloody cerebrospinal fluid is not especially significant as it is not an uncommon finding in spontaneous intracerebral hemorrhage. In *opium poisoning* a clue is generally afforded by the extreme contraction of the pupils and the very infrequent respiration. In *alcoholic intoxication* the coma is rarely so complete as in cerebral hemorrhage and the patient, as a rule, can be aroused by shouting. The odor of alcohol on the breath is, of course, suggestive, but it should not be forgotten that apoplexy sometimes comes on during intoxication. The diagnosis between *uremia* and cerebral hemorrhage is sometimes difficult. Evidences of nephritis (albuminuria, edema, thickening of the arteries, accentuation of the aortic second sound, etc.) do not exclude apoplexy, since the latter not rarely results from nephritis; on the other hand, signs of paralysis are not absolute proof of apoplexy, since it is well known that uremia itself is capable of producing transient hemiplegia. Paralysis, however, is much more frequent in cerebral hemorrhage than in uremia, while the reverse is true of convulsions. The occurrence of albuminuric retinitis is strongly indicative of uremia and so is a marked excess of waste nitrogen in the blood. *Diabetic coma* is distinguished by the sweetish odor of the breath and the presence of sugar and of acetone bodies in the urine. *Epileptic* coma may be recognized by a history of previous convulsive attacks, or, if this is unobtainable, perhaps, by the presence of scars on the tongue. Further, in epileptics the signs of arterial disease are commonly wanting and there are no evidences of paralysis. *Sunstroke* as a cause of coma is suggested by the history of exposure to excessive heat, the high body temperature, and the absence of unilateral paralysis.

The differentiation of *occlusion* of the *cerebral vessels* by *emboli* or *thrombi* is considered on p. 947. The transient hemiplegias and aphasias occasionally observed in *migraine*, *Raynaud's disease* and even in *pregnancy* must not be mistaken for hemorrhagic apoplexy. The loss of function in such cases is explained by a temporary contraction or spasm of the bloodvessels, causing an ischemia.

**Prognosis.**—Cerebral hemorrhage is a grave condition even though it does not always prove fatal. The probability of survival is influenced by the previous condition of the patient, and the location and extent of the bleeding. A second attack is more likely to kill than the first. The existence of Bright's disease makes the outlook especially serious. Hemorrhages into the pons, cerebellum, or medulla, unless extremely small, are almost invariably fatal. During the attack the probable outcome is to be judged by the general severity of the symptoms. Deep coma, especially if protracted for more than twenty-four hours, a marked depression of temperature for several hours after the attack, followed by an elevation to 103° F. or higher, loss of sphincter control, convulsions, conjugate deviation of the eyes and head, and Cheyne-Stokes breathing are all symptoms of unfavorable augury. Even when these phenomena are absent, however, the prognosis should be given with great caution, in as much as there is always danger of the hemorrhage recurring, bursting into the ventricles, and proving rapidly fatal.

The prognosis as to recovery from the paralysis must also be guarded.

It is always probable that some restoration of power will occur, but how much can never be foretold. As a rule, palsy of the face passes off completely and in many cases much motion is regained in the leg. Complete recovery in all parts, however, is very exceptional. Generally speaking, the less extensive the paralysis and the more rapid the improvement, the more complete will be the restoration of function. The persistence of contractures after the lapse of several months usually precludes all hope of further amelioration. Disorders of intelligence continuing for more than a few weeks after an attack are also likely to prove permanent. Finally, when once cerebral hemorrhage has occurred there is always danger of a recurrence, since the underlying etiologic conditions still remain. Many hemiplegics, however, live for five or ten years, or longer.

**Treatment.**—Persons predisposed to cerebral hemorrhage should be advised to lead a life as free as possible from mental excitement and strenuous physical exercise, to abstain from alcohol, to reduce the intake of food, and, as an additional means of keeping down the blood pressure, to secure each day a free evacuation of the bowels, using for the purpose, if necessary, some suitable aperient.

*The Attack.*—Every effort should be made to keep the patient absolutely quiet. If he must be moved, the transportation should be done with extreme gentleness, and the distance reduced to a minimum. The head and chest should be slightly raised. In some cases it may be necessary to draw the jaw and tongue forward to prevent mechanical asphyxia. An ice-bag to the head is useful. A brisk cathartic, such as croton oil (1–2 drops in a little olive oil), may be placed on the back of the tongue to secure prompt catharsis. If the face is congested and the pulse full and strong, venesection to the extent of 8, 10 or 12 ounces is apparently indicated, although Cushing[1] gives experimental evidence to show that the persistent high arterial tension is only an indication of nature's effort to ward off fatal anemia of the bulbar centers brought about by the extreme degree of intracranial tension and that when the blood pressure steadily rises to 250 mm. or higher trepanation is the only measure that holds out any prospect of success. Even if the clot is not found and removed, the relief of the cerebral compression afforded by the operation, it is claimed, may suffice to revive the exhausted bulbar centers, and arrest the alarming symptoms. Important as these observations appear to be, it is doubtful whether they will convince many of the advisability of surgical intervention in any case of cerebral hemorrhage that is not clearly cortical or subcortical.

If the heart action is feeble and the face is blanched diffusible stimulants may be given cautiously, although it is unlikely that they will prove of much value. Thorough cleanliness, bathing with alcohol, frequent change of position, and the avoidance of roughnesses in the bed are necessary in order to prevent the development of bed-sores. Since blisters are produced more readily than in health, special care should be taken in using hot applications of any kind. Retention of urine is likely to occur, and if it does the patient must be catheterized.

Even in the mildest cases the patient should not be allowed to leave his bed for two or three weeks, and during this time the diet should be light and unstimulating. The ice-cap should still be kept upon the head. Aconite is often useful in subduing the fever of reaction and in decreasing arterial tension. For restlessness and wakefulness, small doses of a bromid or of chloral may be given.

*Chronic Stage.*—After the acute symptoms have entirely disappeared,

[1] Amer. Jour. Med. Sci., vol. cxxv, 1903.

which will rarely be earlier than ten days or two weeks after the attack, massage should be systematically practised. It often contributes to the restoration of power, or when this is impossible, to the prevention of contractures. After the lapse of three or four weeks, triweekly applications of the faradic current may be of service.

In some cases warm saline baths (90°–95° F.), combined with passive movements, prove useful adjuvants to massage. Potassium iodid is often prescribed with the hope that it may aid in absorbing the clot, but it is of doubtful utility, and, moreover, it is very prone to disturb the digestion.

## CEREBRAL THROMBOSIS AND EMBOLISM

Thrombosis and embolism of the cerebral arteries arise from conditions that produce the same processes elsewhere in the body.

**Thrombosis** is most commonly due to arteriosclerosis or to syphilitic endarteritis, but it also follows embolism (secondary thrombosis), and very rarely it results from alterations in the blood itself, such as occur in acute infectious diseases and severe anemia. Thrombi form most frequently in the middle cerebral artery or its branches, the basilar, vertebral, anterior cerebral and posterior cerebral arteries.

**Embolism** usually depends upon endocarditis, especially the recurring form which attacks valves already the seat of sclerotic changes, but it may arise from a cardiac thrombus, an aneurysm, or a diseased condition of the aorta or other large arteries. Embolism usually occurs in a branch of the middle cerebral artery or in a branch of the sylvian artery. An embolus cannot plug the basilar artery as its lumen is larger than its branches, although it may lodge at its bifurcation and give rise to an obstructive thrombus. The vessels of the cerebellum are rarely affected either by embolism or thrombosis. Of 131 cases of cerebral embolism studied anatomically by Gelpke, 64 were on the left side, 54 on the right side, and 13 on both sides.

The occlusion of a cerebral artery by an embolus or thrombus is followed, as a rule, by liquefaction necrosis on softening of the area supplied by the vessel involved. The appearance presented by the dead area varies with the amount of blood effused and the age of the necrotic process. The admixture of a large amount of blood with the disintegrated tissue produces *red softening*, whereas the complete exclusion of blood from the dead focus (*anemic infarct*) results in *white softening*. Difference in color, however, may be due merely to difference in age, since red softening in time may become white, through absorption of the blood-pigment. *Yellow softening* is really only a later stage of red softening. Microscopically, the disintegrating mass consists of fragments of nerve-fibers and nerve-cells, droplets of myelin, compound granule cells, fat drops, and a variable amount of blood-pigment. Reparative changes may follow, as in cases of cerebral hemorrhage, and ultimately the dead focus may be replaced by a cyst or cicatrix. Secondary degenerations, like those appearing after hemorrhage, may also occur.

**Symptoms.**—In many cases of thrombosis and embolism the symptoms are the same in all respects as those of hemorrhage and a differentiation is impossible. Not rarely, however, there are certain indications that point more or less clearly to one or another of the three conditions, and of these only will it be necessary to speak. Prodromes for a few days before the attack, such as headache. vertigo, transient aphasia, or passing weakness in the members afterward paralyzed are more suggestive of thrombosis than hemorrhage. The appearance of the symptoms during sudden exertion points to hemorrhage, while their occurrence during a period of weakness or mental

depression points rather to thrombosis. Apoplexy occurring during sleep is more frequently the result of thrombosis than of hemorrhage. A history of a number of preceding slight attacks is strongly indicative of thrombosis. Chronic nephritis is more favorable to hemorrhage than to thrombosis, while the reverse is true of syphilis. Unconsciousness may be due to either condition, but preservation of consciousness is much more common in thrombosis than in hemorrhage. Slowly increasing unconsciousness ending in profound coma (ingravescent apoplexy) is usually the result of hemorrhage. A sudden onset with persistent coma, facial cyanosis, stertorous breathing, an infrequent, full pulse, and marked depression of temperature during the first day or two make the occurrence of hemorrhage highly probable, but the absence of these features has little negative weight.

In embolism there are no premonitory symptoms; the onset is sudden; coma is frequently absent, and if present, usually of short duration; the respiration is rarely stertorous; the pulse is more often weak than strong; and initial temperature changes are slight, although fever may develop about the third day. The patient may be of any age, but very frequently he is comparatively young and shows no evidence of arterial degeneration. He does present, however, with rare exceptions, the signs of aortic or mitral valvular disease, which is the usual source of emboli that lodge in the vessels of the brain. Of course, valvular disease frequently coexists with conditions that are favorable to hemorrhage or thrombosis, and, therefore, it need scarcely be added, the mere presence of a cardiac murmur can never justify the diagnosis of embolism, if the cerebral symptoms point strongly to either of the other lesions.

**Treatment.**—When symptoms are present in a case of cerebral apoplexy that make the occlusion of an artery more probable than extravasation of blood, the treatment should consist in absolute rest, in the use of mild circulatory sedatives or stimulants according to the condition of the pulse, and, if there is much restlessness, the administration of bromids. Venesection is contraindicated. The management of the patient after the attack is that of the chronic stage of cerebral hemorrhage (see p. 946).

## INTRACRANIAL SINUS THROMBOSIS

Thrombosis of the cerebral sinuses occurs in two forms—the marantic and the infective.

**Marantic thrombosis** usually affects the *longitudinal sinus* and its tributary veins. It occurs in anemic and cachectic states, especially when these are associated with pronounced cardiac weakness, and is most common at the extremes of life.

The symptoms are often overshadowed by those of the primary condition. Distention of the veins of the scalp, headache, mental dulness, epistaxis, retraction of the head from meningeal irritation, general convulsions, and local spasms and paralyses, especially in the legs, are the most common manifestations. The outlook is grave, although resorption of the clot seems to be possible.

**Infective thrombosis** affects chiefly the paired sinuses and is most common in adults. The sinus nearest to the infective atrium is the one that is usually involved. The thrombus is, as a rule, soft and necrotic and is frequently accompanied by purulent leptomeningitis, cerebral or cerebellar abscess and septicopyemia.

*Infective lateral sinus thrombosis* is especially common and is dependent in the vast majority of cases upon septic infection in the middle ear, although it may be secondary to septic processes elsewhere. Of 128 cases of sinus thrombosis analyzed by Allport,[1] 118 had their source in suppurative otitis media. The usual local indications are pain, tenderness, edema over the mastoid and in the upper part of the posterior cervical triangle, distention of the regional veins, engorgement and induration of the external jugular

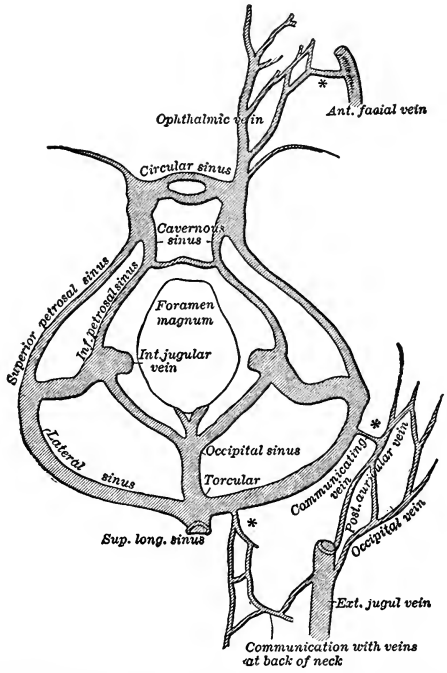


FIG. 33.—Diagram showing the communications existing between the lateral and cavernous sinuses and the external veins, indicated in the figure by * (Leube).

vein, or if the internal jugular alone is occluded, abnormal emptiness of the external vein (Gerhardt's sign), inclination of the head to the affected side, and enlargement of the cervical lymph-nodes. Symptoms referable to pressure on various cranial nerves are not uncommon and choked disc may occur. The general symptoms are those of septicemia and include fever, sweats, chills, and polymorphonuclear leucocytosis. Unless surgical treatment proves effectual, death usually ensues within a few days, but a much longer course is sometimes observed, and in very rare instances there is spontaneous recovery. Opening of the sinus and removal of the thrombus is successful in many cases.

[1] Jour. Amer. Med. Assoc., 1902, p. 690.

*Infective cavernous sinus thrombosis* occurs in connection with septic nasal or orbital disease, traumatic injuries of the cranial and facial bones, facial erysipelas, anthrax, etc. The manifestations are usually unilateral at first, but are prone to become bilateral. The most common indications are pain in the head, especially in the supra-orbital or infra-orbital region, edema and venous congestion about the eye, conjunctival ecchymosis, exophthalmos, paralysis of the ocular muscles and choked disc. Symptoms of septicemia are also present. The condition is almost invariably fatal, although in one or two instances surgical intervention has been successful.

## TUMORS, INFECTIOUS GROWTHS AND PARASITIC CYSTS OF THE BRAIN

The substance of the brain is not only a seat of primary growths, but it is often invaded secondarily by growths originating in the meninges and cranial bones. Of the true neoplasms affecting the brain, the most frequent are gliomata, endotheliomata and sarcomata. Carcinomata, cholesteatomata, fibromata and angiomata are occasionally observed. Of the infectious growths, the most important are tuberculomata and gummata. Parasitic cysts are rare, but cysticercus cellulosæ (larval state of the pork tapeworm) and echinococcus cysts are sometimes found.

**Gliomata.**—These are tumors composed of neuroglia-tissue. According as the cells or the delicate fibrillæ predominate, two varieties may be distinguished, the *hard* and the *soft*. The former, which is comparatively rare, arises from the subependymal layer of the ventricular wall and projects into the ventricles. The latter, the commonest of all brain tumors, usually appears as a diffuse infiltrating growth, resembling more or less closely the brain substance in which it is imbedded. The color is grayish or reddish, depending upon the vascularity of the tissue and the presence or absence of hemorrhage. The consistence may be about the same as that of the normal brain, but it is often more pulpy, owing to retrograde changes. Occasionally, circumscribed and even encapsulated forms are encountered. Histologically, gliomata are composed of adult glia cells (spider cells) and a more or less abundant fibrillar ground-substance, or of numerous round cells of embryonic type and very few radiating processes or fibrils (so-called *gliosarcoma*). In some cases ganglion cells are present (*ganglionic neuroglioma*), and in others the cells are of ependymal type (*ependymal glioma*). Gliomata are most commonly found in the cerebral hemispheres, but occur also in the cerebellum and brain stem. They rarely invade or perforate the meninges and do not give rise to metastases. Necrosis with cavity formation and hemorrhagic extravasation into their substance, from the rupture of the delicate vessels in which they frequently abound, are common occurrences. Owing to their slow growth and tendency to push the nerve fibers aside before destroying them, they often exist for a comparatively long time without producing serious disturbances.

**Endotheliomata.**—These are benign tumors of slow growth, arising from the endothelial lining of the meninges or, more rarely, from that of the cerebral bloodvessels, large sinuses or lymphatics. They often appear as multiple, separate or coalescing nodules. The cells are likely to assume a spindle form from pressure, but a variable number of flat polyhedral cells with clear cytoplasm, a small pale nucleus and minute nucleoli, and arranged concentrically around vascular channels may usually be found. Even when the

prevailing cell is spindle-shaped the discovery of a few endothelial cells with the characters above described and an absence of fibrils will serve, as a rule, to exclude sarcomata and fibromata. Endotheliomata impress themselves into the brain, but do not infiltrate it, and in most of the cases shell out easily. The cerebello-pontine angle is a favorite site.

**Sarcomata.**—These are less common than either gliomata or endotheliomata. When primary they arise from the membranes or from the cranial bones. Ordinarily, they are circumscribed or even encapsulated, and surrounded by a zone of softened brain tissue, which makes their removal comparatively easy. Secondary sarcomata are frequently found within the brain, especially the subcortical portion of the hemispheres, and are usually multiple. General metastases, however, are not observed.

**Carcinomata.**—These tumors are almost invariably secondary to primary growths in the mammary glands or internal organs. The metastasis is multiple in about one-third of the cases and usually affects the cerebrum. Primary malignant adenoma sometimes occurs in the pituitary body and primary papillary carcinoma in the ependyma of the ventricles.

**Cholesteatomata.**—These appear as small, glistening, waxy bodies composed of concentric layers of squamous epithelial cells and variable amounts of sebaceous material and cholesterin. They arise from embryonal epidermal inclusions (Bostroem, Bonorden) and are therefore of the nature of dermoid cysts. They are connected with the meninges and have a predilection for the base of the brain.

**Tuberculomata.**—Circumscribed tuberculous masses may occur on the surface of the brain, secondarily to a focal lesion of the meninges (*focal tuberculous meningoencephalitis*), or in the substance of the brain, especially in the cerebellum or brain-stem, as a result of direct hematogenous implantation (*solitary tubercles*). In either case, but particularly in the latter, the symptoms may be those of tumor. Solitary tubercles, or more correctly conglomerate tubercles, are generally rounded or irregular masses, varying from the size of a small pea to that of a goose-egg, and consisting of yellowish-white cheesy matter, surrounded at times by an inflammatory zone studded with fresh tubercles. Liquefaction or calcification may occur as in tuberculous lesions elsewhere. Tuberculomata are common forms of growth and are met with most frequently in childhood. In nearly 20 per cent. of the cases tabulated by Starr they were multiple.

**Gummata.**—These also occur with considerable frequency, but unlike tuberculomata rarely develop in childhood. In the large majority of cases the lesion assumes the form of a more or less circumscribed caseous meningitis or meningoencephalitis affecting the base of the brain or the convexity of the hemispheres. Solitary gumma of the brain substance is relatively rare. When of recent origin, syphilitic deposits are soft, gelatinous, and of a grayish or grayish-red color. Through caseation they become dry, yellow and fairly firm, and later absorption and fibrosis are likely to occur, transforming them into thick cicatrices.

**Parasitic Cysts.**—Echinococcus cysts are rarely found in the brain even in countries in which infestation with Tænia echinococcus is most prevalent. The cysts grow slowly, but in time may reach a large size and give evidence of their location by causing resorption of the overlying bone.

Cysts produced by the larva of Tænia solium (cysticercus cellulosæ), though of rare occurrence in man, are relatively frequent in the brain and seem to have predilection for the wall of the fourth ventricle. In many cases they are multiple.

**Etiology.**—The frequency of intracranial growths cannot be definitely stated, but it is probably not much less than 1 per cent. Although no age is immune, the period of greatest incidence is between 15 and 40 years. Males are affected more frequently than females. Heredity has little or no influence. Trauma appears to be a factor of some importance. It may be the direct exciting cause of the tumor or it may merely accelerate the growth of a previously existing tumor.

**Effects of Cerebral Tumors.**—The injuries set up and the disturbances induced by brain tumors are usually the result of a number of factors: (1) a general increase in the intracranial pressure; (2) direct irritation or destruction of the tissues; (3) secondary degeneration of the tissues from compression of bloodvessels or separation of nerve-fibers from their genetic centers; (4) hyperemia or inflammation of surrounding tissues; (5) edema of the brain from vascular stasis; and (6) obstructive hydrocephalus.

In individual cases the clinical manifestations vary in accordance with the location, size, shape, nature, rapidity of growth and vascularity of the tumor. A marked fluctuation in the symptoms from time to time is often observed in the same case, owing to changes in the circulation, hemorrhages, variations in the tension of the cerebrospinal fluid, and, perhaps, the sudden inhibition of function in nerve-centers widely separated from the center in which the tumor is located, but in some way physiologically related to it—the so-called "diaschisis" of von Monakow.[1]

**Symptoms.**—In the majority of cases two groups of symptoms may be recognized, one occurring irrespective of the situation of the tumor and resulting from increased intracranial pressure (*general symptoms*), the other depending upon irritation or destruction of parts possessing definite functions (*focal symptoms*). In some instances only one group is present, and occasionally tumors are found post-mortem that have given no evidences whatever of their existence during life.

## General Symptoms

*Headache* is the most constant symptom and often the first of which the patient complains. It is usually frontal or occipital, without reference to the seat of the lesion. Only in superficial growths is it likely to be definitely localized. It varies in intensity from a sensation of fulness to agonizing pain and may be persistent or paroxysmal. In some instances the attacks are indistinguishable from those of migraine. Tenderness to pressure occasionally accompanies the pain when the tumor is immediately beneath the cranium. *Optic neuritis* or *choked disc* (see p. 910), occurs sooner or later in more than 75 per cent. of the cases. It is usually bilateral, though often more marked on one side than the other. In the majority of cases it is, perhaps, more intense on the side of the tumor, but according to Paton,[2] who has analyzed about 400 cases, the difference is too slight to be of much localizing value. Although choked disc does not depend entirely upon the location of the tumor, it is almost constant in subtentorial tumors and relatively uncommon in tumors of the meninges, of the white matter of the cerebral hemispheres, and of the pons. It is absent in glioma more frequently than in any other tumor. The important fact should not be forgotten that severe optic neuritis is compatible with fairly good vision if optic atrophy has not commenced. Examinations made by Bordley and Cushing[3] indicate that

[1] Die Lokalization im Grosshirn u. der Abbau der Funk. durch Kort. Herde, Wiesbaden, 1914.

[2] Brain, 1909, xxxii, No. 125.

[3] Archives of Ophthalmology, Sept., 1909.

inversion or interlacing of the color fields (*dyschromatopsia*) occurs almost as frequently as neuroretinal edema and may appear before the latter.

*Psychic disturbances*, such as listlessness, impairment of memory, slowness in thinking and talking, and various degrees of dementia, are noted in many cases and are probably referable to the increased intracranial pressure. So too, *general convulsions* may occur with tumor in any part of the brain, the only convulsions available for the localization of the lesion being those that are confined to definite portions of the body or that uniformly begin in one particular member. *Vomiting* occurs in one-fourth of all cases. Though it is a late symptom, as a rule, it may be an early indication, especially in children, in whom, too, it is relatively common. In many cases the attacks are excited by changes of position and bear no relation to the taking of food. Nausea may or may not be present. When the headache is severe the vomiting may be projectile. *Vertigo* is not unusual, but it is rarely pronounced except in infratentortial lesions affecting the vestibular apparatus. *Loss* of *weight*, not wholly referable to the vomiting, pain or wakefulness, is sometimes a prominent symptom. The *cerebrospinal fluid* is often excessive and may accumulate with extraordinary rapidity after evacuation. Other general manifestations occurring more or less frequently are *changes in the pulse rate, irregular respiration, elevation of temperature, somnolence* or *insomnia*, and *polyuria*.

## Focal Symptoms

*Frontal Lobes.*—Mental symptoms may be associated with tumors in any part of the brain, but they seem to be especially frequent and pronounced when the region in advance of the generally accepted motor area is affected. The most prominent psychic features are a change of disposition, slowness of cerebration, forgetfulness, particularly for recent events, loss of power of attention, rambling speech, morbid wittiness (Witzelsucht), and lastly, a state of dementia with loss of cleanly instincts. Drowsiness, with periodic attacks of stupor, is not uncommon. The sense of smell is sometimes lost. From infringement of the tumor on the adjacent motor centers or their efferent fibers attacks of *petit mal* or of Jacksonian epilepsy may occur or there may be contralateral hemiparesis with increased deep reflexes, diminished abdominal reflexes, and an extensor plantar reflex. Tumors in the posterior part of the left frontal lobe are sometimes attended by motor aphasia. A fine tremor of the limbs homolateral to the growth has been noted in a number of cases. Kennedy[1] considers the occurrence of true retrobulbar neuritis, with the formation of a central scotoma and primary optic atrophy on the side of the lesion, together with concomitant papilledema in the opposite eye, a symptom-complex of decisive diagnostic significance and observed it in 6 cases, 5 of which were proved by operation. Paralysis of the motor cranial nerves or sensory disturbances rarely occur except as a result of indirect pressure.

*Temporal Lobe.*—Tumors in this situation often fail to produce focal symptoms. Word-deafness, however, may be present if the lesion involves the first temporal convolution of the left side in a right-handed person. Invasion of the uncinate gyrus may be indicated by the occurrence of the seizures described by Hughlings Jackson as the *uncinate type of fits*. These consist of subjective sensations of smell and taste, vague epigastric sensations, movements of the lips, tongue, jaws, and associated parts, and a peculiar "dreamy state." Salivation and partial asphyxia have also been noted in

[1] Amer. Jour. Med. Sci., Sept., 1911.

some of the attacks. Generalized epileptic seizures seem to be especially common in lesions involving the temperosphenoidal lobe.

*Corpus Callosum.*—Motor apraxia of the left side is an important focal symptom of tumors of the corpus callosum, at least of its anterior part. Movements may be correctly performed on occasion, but not when the patient wishes to do so. Instead of the intended movement being executed, the preceding one may be repeated (perseveration) or the movement, although correctly performed, may be transferred to an entirely different musculature (parapraxic movement). Accompanying the apraxia, there may be pronounced impairment of intellect and a gradually developed hemiparesis, first on one side and then on the other, and affecting the legs more than the arms. Marked paresis interferes, of course, with the recognition of the apraxia.

*Motor Area.*—If the tumor is small and irritates the cortex the chief manifestation is the occurrence of contralateral spasms confined to one limb or one side of the face, or beginning in one part and then extending to other parts represented in adjacent cortical centers, until finally, perhaps, the movements become unilateral or even general (Jacksonian epilepsy). Such attacks are usually accompanied by numbness and tingling in the part first affected and are often followed by temporary paresis. The point at which the convulsion begins is a clue to the situation of the lesion. As the growth enlarges the paresis may become permanent and extend in the same orderly way as the spasm. Consciousness is usually retained, although occasionally it is lost before, during or at the conclusion of the attack. In exceptional cases continuous twitching of an arm or leg (epilepsia continua) takes the place of periodic Jacksonian spasm. It must be borne in mind that monospasm or hemispasm may result from tumors in parts of the brain other than the motor cortex and may occur with lesions other than tumor, such as localized hemorrhage, meningoencephalitis, sclerosis, etc., and even with idiopathic epilepsy.

Occasionally spasms are absent in tumors of the motor region and the only indication is a gradually developing hemiplegia or, more rarely, monoplegia. The reflexes on the paralyzed side are exaggerated and if the lesion is in the leg center Babinski's phenomenon is present. If other focal symptoms occur they are due to compression or invasion of adjacent areas with other functions.

*Parietal Region.*—Tumors in this region frequently cause contralateral disturbances of the various forms of sensation, such as diminished sensibility to touch, pain, and temperature, impairment of the senses of position and movement, hemiataxia, inability to recognize objects by handling them (astereognosis[1]) and paresthesias. If the tumor is deep-seated and destroys the fibers of the optic radiation hemianopsia will be present; if it is on the left side and invades the angular gyrus there will be word-blindness; and if it encroaches upon the anterior central convolution it may cause Jacksonian spasms with sensory auræ and hemi- or monoparesis.

*Occipital Lobe.*—The most important focal symptom of tumors in this region is a loss of both right or of both left visual fields (lateral homonymous hemianopsia). The lesion is on the opposite side of the dark fields. The pupillary response to illumination is intact for the entire retina, whereas in hemianopsia dependent upon disease of the optic tracts a reaction is said to be obtained only when the seeing half of the retina is illuminated (Wernicke's hemianopic pupillary reaction). Visual hallucinations sometimes occur in the hemianopic field. Lesions of the left occipital lobe in right-

[1] The stereognostic sense is a complex of tactile, muscular and arthritic memories of movements (Horsley).

handed persons may also cause so-called mind-blindness, or inability to recognize the significance of familiar objects by the sense of vision.

*Thalamus.*—The most definite symptoms of thalamic tumor are persistent hemiparesis, usually flaccid; persistent hemihypesthesia; hemiataxia and astereognosis; distressing pains of an aching or burning character; and lateral hemianopsia, all of which are on the side contralateral to the lesion. As neighborhood symptoms choreo-athetoid movements may occur through involvement of the striate body, permanent hemiplegia with contracture through involvement of the internal capsule, and oculomotor symptoms through involvement of the quadrigeminal bodies.

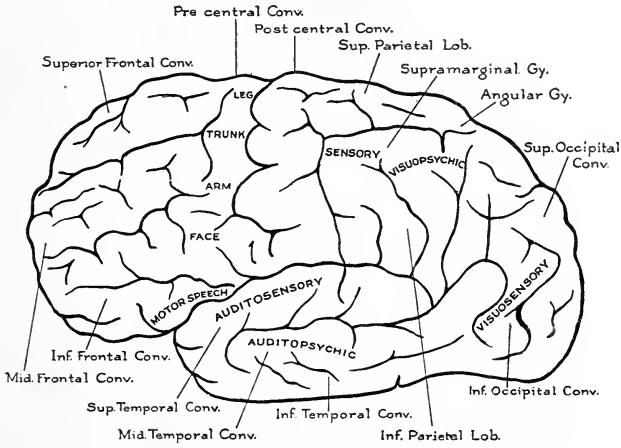


FIG. 34.—Functional areas of cerebral cortex of the left side (after Campbell).

*Corpus Striatum.*—Gross lesions of the corpus striatum, by involving the internal capsule, are usually productive of hemiparesis on the side contralateral to the lesion. According to Hunt,[1] lesions that destroy the globus pallidus result in paralysis agitans, while those involving the other nuclei manifest themselves in choreic movements.

*Pons.*—Circumscribed solitary growths in the pons frequently produce paralysis of one or more of the cranial nerves, more especially of the facial, trigeminus or abducens, on the side of the lesion and spastic paralysis of the limbs on the contralateral side (crossed hemiplegia). In many cases there is also hemianesthesia, partial or complete, on the side of the hemiplegia (crossed hemianesthesia). On the other hand, infiltrating growths usually cause bilateral disturbances, both in regard to the limbs and the cranial nerves. Many combinations of unilateral and bilateral palsies are met with, but according to Bruns all of them may be arranged in four groups: (1) Bilateral paralysis both of cranial nerves and extremities; (2) bilateral paralysis of cranial nerves with unilateral paralysis of the extremities; (3) unilateral paralysis of the cranial nerve with bilateral paralysis of the extremities; (4) bilateral cranial nerve paralysis without involvement of the extremities. Paralysis of the associated lateral movements of the eyes (sixth pair) without

[1] Brain, 1917, 40, 58.

involvement of the vertical movements (third and fourth pairs) is an especially common and significant ocular defect. Choked disc only occurs in about half the cases and is usually late in appearing.

*Crus Cerebri.*—Tumors limited to the crusta may produce a very characteristic syndrome, namely paralysis of the third nerve on the side of the lesion and hemiplegia of the contralateral side. In many instances, however, the oculomotor palsy is observed on both sides. Tumors of the tegmentum are likely to cause alternating sensorimotor paralysis and paralysis of the ocular movements, except those of laterality. Tremors have also been noted in some instances (Benedict, Henoch, Blocq and Marinesco, Holmes, Cushing).

*Corpora Quadrigemina.*—The symptoms that suggest involvement of these bodies are a staggering gait resembling that occurring in cerebellar disease and limitation of the associated movements of the eye, especially the upward and downward movements (partial ophthalmoplegia). Nystagmus is sometimes noted. Disturbances of sight and hearing may also occur if the lateral geniculate bodies are invaded, and complete ophthalmoplegia with contralateral hemiplegia if the crura are implicated. Tumors of the corpora quadrigemina give the highest percentage of choked disc (Weeks and Martin).

*Cerebellum.*—The same general symptoms occur in cerebellar as in other intracranial tumors, but the *headache* is prone to affect the suboccipital region and to extend down the back of the neck, *vertigo* is more common than in supratentorial growths, and *choked disc* is present in a very large proportion of cases. *Nuchal stiffness* or backward retraction of the head sometimes accompanies the headache. *Nystagmus* is frequently present, but whether it is ever a true cerebellar symptom is somewhat doubtful. The most characteristic of all the manifestations of cerebellar tumor, however, is asynergy, or a loss of the power by which movements more or less complex, but functionally definite, are associated in a special act or acts (Mills). The asynergy expresses itself in ataxia, dysmetry or hypermetry, adiadokocinesis, tremor, muscular hypotonia and intermittent asthenia.

The *ataxia* is well shown in the gait, the patient in walking tending to lurch forward or backward or to one side, or to project one shoulder or one side of the body in a given direction, to the right or to the left. If the asynergy affects especially the pelvic girdle the patient in walking may hold the trunk erect and the arms outstretched, keep the feet far apart, and throw the legs forward and outward. The head usually maintains the same plane as the trunk, but not rarely it is tilted or rotated to one side so that the ear approximates one shoulder. The ataxia of movements is not increased by shutting the eyes (negative Romberg sign) and in unilateral tumors usually manifests itself especially on the side of the lesion.

The mismeasurement of movements (*dysmetry* or *hypermetry*) may be demonstrated by the finger-to-nose test. In making the effort the finger may go well beyond the nose or the movements may be of much wider range than normal and include the whole arm and shoulder. *Adiadokocinesis*, an inability to perform movements in rapid succession, is brought out by attempts at alternate pronation and supination of the forearm and hand and is shown in lateral or vertical overmovement. This disturbance, also, an found on the side of the lesion. *Cerebellar tremor*, which is volitional and due to defective coördination of voluntary movements, is observed in efforts to grasp an object and in making the finger-to-nose test. Hunt[1] has described a generalized volitional tremor, which begins locally and

[1] Brain, Oct., 1914.

gradually progresses. Mills and Weisenburg[1] have drawn attention to asynergy of the movements of the tongue, vocal cords, and throat, resulting in a peculiar jerky speech and difficulty in mastication and deglutition.

The *hypotonia* and *asthenia* may be due, as Luciani[2] has suggested, to a loss of sthenic and tonic functions possessed by the cerebellum, or the former may be due to the exhaustion resulting from efforts to perform synergic movements and the latter to the failure of tonectic stimuli from the cerebral cortex to combine rhythmically with unsynergized movements (Mills).

Owing to the position of the cerebellum, tumors originating in it frequently involve adjacent structures, such as the cranial nerves, particularly those from the fifth to the twelfth, and the pyramidal tracts. Involvement of the motor fibers—paresis of the limbs, increased reflexes, Babinski's phenomenon—usually indicates a lesion in the pons or the cerebellopontile angle. Vertigo is common, but it is an *extracerebellar* symptom and indicates implication of the vestibular apparatus. The Bárány method of investigation by means of the caloric and turning tests is of value in differentiating between labyrinthine disease and cerebellar or cerebellopontine tumor.

*Cerebellopontine Angle.*—Tumors in this area grow from the cranial nerves, usually the eighth nerve, or from the cerebellum or, more rarely, the pons. Symptoms referable to involvement of the cranial nerves may be the only focal indication of tumor, but in many cases motor or motor and sensory symptoms from involvement of the pons and a variable degree of asynergy for involvement of the cerebellum are also present.

*Hypophysis Cerebri.*—Lesions of this gland produce in some cases the symptoms of acromegaly and in others the syndrome known as *dystrophia adiposogenitalis*, which consists of sexual infantilism, amenorrhea in women and impotence in men, excessive deposition of fat and hypotrichosis. Owing to the pressure of the tumor on the optic chiasm, impairment of vision, usually in the form of bitemporal hemianopsia (40 per cent. of the cases), but sometimes in the form homonymous hemianopsia (Cushing), is likely to supervene. Optic neuritis occurs twice as frequently when acromegaly is present as when it is absent. Headache is usually severe.

*Pineal Gland.*—Tumors of this body cause almost the same symptoms as tumors of corpora quadrigemina. In the former, however, nystagmus is more common and involvement of the oculomotor, trochlear, and abducens nerves is less common. In a number of cases occurring in children premature development of the primary and secondary sex characters, overgrowth of the body and mental precocity have also been observed.

**Diagnosis.**—While the diagnosis of cerebral tumor is sometimes an easy matter, there are many cases in which the symptoms are obscure and ambiguous. Important points to be considered in reaching a positive opinion are the gradual development of disturbances indicating an increase of intracranial pressure (headache, choked disc, etc.) the orderly appearance or suggestive combination of focal symptoms, and the absence, oftentimes, of definite etiologic factors. Ordinary roentgenography is occasionally of value in showing local changes in the skull, or, if the tumor is calcified, even a definite shadow. It has been especially helpful in the diagnosis of hypophyseal growths. Roentgenography after intraventricular or intraspinal injections of air, or after both injections (pneumography), while by no means free from danger, yields more precise information, the changes that it reveals in the spaces of the brain not rarely leading to a correct diagnosis and localization of the intracranial lesion.

[1] Jour. Amer. Med. Assoc., Nov. 21, 1914.
[2] "Das Kleinhirn," 1893.

Among the organic diseases of the brain which may be confused with tumor are abscess, intracranial aneurysm, paretic dementia, and disseminated sclerosis.

In *abscess* the symptoms are more likely to be remittent than in tumor, an acute stormy onset being followed in many instances by a long period of relative or absolute quiescence; choked disc is less frequent; fever and leucocytosis are sometimes present, especially in the early stages; and still more important, a definite cause, such as trauma, otitis media, disease of the accessory sinuses of the nose, bronchiectasis or empyema, can usually be demonstrated.

*Intracranial aneurysms* have rarely been recognized during life. Of 555 cases analyzed by Beadles,[1] in about one-third no symptoms whatever were present, in more than half the first symptoms were those of cerebral apoplexy, and in the remainder the symptoms were indistinguishable from those of tumor. A bruit has little diagnostic value, since it is usually absent in aneurysm and is occasionally heard in tumor. Subjective hissing and buzzing sounds are also fallacious.

*Paretic dementia* may produce a picture very similar to that of tumor of the frontal lobes, but in the former there is no choked disc and headache is not a special feature. Moreover, the presence of the Argyll-Robertson pupil, of a drawling tremulous speech, of unfounded euphoria, of grandiose delusions, of concomitant tabetic symptoms, and of definite changes in the cerebrospinal fluid (pleocytosis, increase of protein, positive Wassermann reaction, positive colloidal gold reaction, etc.) usually make the distinction clear.

*Disseminated sclerosis* is at times difficult to distinguish from tumor of the cerebellum and midbrain. Pallor or atrophy of the optic disc, a scanning or staccato speech, emotional alterations, disorders of micturition, bilateral spastic paralysis and superficial sensory disturbances point to the former, while optic neuritis or choked disc, severe headache, and pronounced asynergy are strongly in favor of the latter.

It is commonly impossible to differentiate a true tumor of the brain from the condition known as *pseudo-tumor*, which is apparently a form of hydrocephalus due to serous meningitis and capable of spontaneous recovery. An acute onset with rising temperature and frequent fluctuations in the intensity of the symptoms suggest serous meningitis, while a gradual onset without fever and a continuous slow increase of the symptoms speak more for a true tumor, although as the latter is often accompanied by hydrocephalus, it may also produce symptoms which show great variations in intensity.

*Hysteria* may simulate cerebral tumor very closely, but the presence of optic neuritis, loss of pupillary reflexes, paralysis of the cranial nerves, a plantar reflex of the extensor type, Jacksonian fits, or other signs of organic disease will usually place the diagnosis beyond all doubt. Occasionally certain general conditions, such as *severe anemia*, *uremia* and *chronic plumbism*, bear a more or less close resemblance to tumor of the brain.

The *nature of the tumor* may be very apparent, but, as a rule, it can only be surmised. The important points to be considered in forming an opinion are the family history, the age of the patient, the presence or absence of cancerous, syphilitic or tuberculous foci in other parts of the body, and the situation of the growth, if this can be ascertained.

**Prognosis and Course.**—The prognosis in cerebral tumors is very grave. Internal medication, except in some syphilitic cases, yields at best only palliative results and extirpation of the growth is indicated in but a small proportion of cases. In general, the course is steadily progressive, although

[1] Brain, 1907, xxx, 285.

a striking remission in the symptoms for a more or less prolonged period is sometimes observed and in very rare instances retrograde changes in the tumor may bring about a spontaneous cure. On the other hand, death may occur suddenly and unexpectedly at any time from hemorrhage into the growth, acute edema of the brain, or strangulation of the medulla at the foramen magnum. The average duration of the disease is probably not longer than 2 or 3 years.

**Treatment.**—If there is the slightest doubt as to the nature of the growth vigorous antisyphilitic treatment should be instituted. In this connection it is well to remember three facts: First, that gummata do not always yield to arsphenamin, mercury and iodids; second, that improvement under these remedies is not positive proof of the gummatous nature of the lesion, because a temporary amelioration of symptoms may also occur in other tumors, notably in gliomata, under antisyphilitic treatment; and third, that a syphilitic person may have a non-syphilitic tumor. In the absence of urgent symptoms, the antisyphilitic treatment should be continued for several weeks, then if no decided improvement is observed and the tumor is in an accessible region (near the surface of the cerebrum, in a lateral lobe of the cerebellum, at the side of the cerebellum and pons, in the neighborhood of the hypophysis), and is clearly not metastatic, operation is indicated as an *extirpatory measure*, for the risks of operation in competent hands are much less serious than those of delay. The more strongly the evidence supports the belief that the tumor is single, circumscribed and benign the greater are the probabilities that a cure will result. In the hands of those having the requisite skill the operative mortality may be less than 10 per cent. In a series of 136 cases reported by Cushing[1] the operative mortality was 7.3 per cent., complete recovery occurred in about 5 per cent., recovery with some persistence of symptoms in 10 per cent., and alleviation of symptoms and prolongation of life in 50 to 60 per cent. In series of 112 cases (197 operations) reported by Magnus[2] the operative mortality was 8.2 per cent., clinical cure occurred in 10 per cent., and improvement in 50 per cent. As regards the nature of the tumor, endotheliomata are most often operable and gliomata and metastatic growths are least often operable.

Even when extirpation of the tumor is not feasible craniectomy (*decompression*) over a "silent" area and in a region where adequate muscular support can be given to the bulging brain (right subtemporal and suboccipital regions) is often advisable with the view of saving sight, relieving distress and prolonging life. *Radium* or *x-ray therapy* combined with craniectomy has occasionally given good results, especially in pituitary lesions.

*Lumbar puncture* is also of some value as a decompressive measure, but it must be employed with great caution, for sudden death may follow the removal of a large amount of fluid, the increased intracranial tension causing the medulla to be forced against the foramen magnum when the intraspinal pressure is relieved.

Except in syphilitic growths, the *medical treatment* of brain tumor is merely palliative. Headache may be relieved to some extent by the administration of coal-tar analgesics in large doses, by the application of ice-bags to the head, and, at times, by the application of dry or wet cups to the back of the neck. The administration of ergot has also been recommended. Eventually, morphin must be given, although it, too, may fail unless the dose is large enough to cause stupefaction. Vertigo and vomiting are sometimes benefited by the administration of bromids or of scopolamin.

[1] Jour. Amer. Med. Assoc., 1915, vol. 64.
[2] Norsk. Mag. for Laegevidenskaben., 1921, No. 9.

## ABSCESS OF THE BRAIN

**Etiology.**—By far the most common cause of intracranial abscess is the direct or indirect extension of a suppurative process to the brain from contiguous structures, notably the tympanic cavity and mastoid cells, accessory nasal sinuses, orbit, and other cranial bones. In from one-third to one-half of all cases the primary affection is *purulent otitis media*, usually chronic, but occasionally acute, the infection reaching the brain by way of the perivascular lymphatics, by the veins, or by direct extension from the diseased bone. In a series of 570 cases of otitic origin, reported by Heimann[1] 80 per cent. were due to chronic otitis media and 20 per cent. to acute otitis media. *Frontal sinusitis* was the cause of the abscess in 8 of 26 cases examined at the Mayo Clinic (Adson[2]). Another and frequent source of the disease is found in various *traumatic injuries* to the head, such as fractures of the cranial bones, open wounds of the soft parts, and even simple contusions. The interval between the accident and the development of the abscess is rarely less than a week (acute traumatic form) and it may be many weeks or months (chronic traumatic abscess). Not infrequently, the disease is *metastatic*, the infected embolus producing it coming from a remote focus of suppuration, which in the large majority of cases is chronic and situated in the respiratory tract. The associated pulmonary condition may be empyema, abscess, bronchiectasis or rarely tuberculosis. Metastatic abscess of the brain is often multiple, but in the absence of general pyemia it may be single. Occasionally, intracranial suppuration occurs as a complication or sequel of an *acute specific infection*, such as erysipelas, typhoid fever, pneumonia, cerebrospinal fever, and influenza. Finally, in rare instances the process must be designated cryptogenic, as the origin of the suppuration cannot be explained.

Males are more subject to abscess of the brain than females and more than one-half of all cases occur between ages of 10 and 30 years.

**Morbid Anatomy.**—Solitary brain abscesses are generally situated in the cerebrum or cerebellum, the former being involved about four times as frequently as the latter. The pons and medulla oblongata, owing to their protected position, and remoteness from the various cavities and sinuses of the skull, are rarely implicated. Otitic abscesses are nearly always either in the temporosphenoidal lobe or in the cerebellum, the relative frequency of the former to the latter site being as three to one. Rhinogenic abscesses are usually found in the adjacent frontal lobes. Metastatic abscesses show a predilection for the area supplied by the left sylvian artery. Abscesses due to trauma are likely to be superficial and to correspond to the point of injury, although not rarely they are on the opposite side of the brain. Unless the brain is actually penetrated the collection of pus is usually subdural or extradural rather than intracerebral (Ballance).

The average size of an encephalic abscess is about that of a walnut. The pus may be thin or thick and of a yellowish or greenish hue. In the case of ear disease, it is often intensely fetid. Acute abscesses have no delimiting membrane and are surrounded by an area of inflamed and softened brain tissue; the more chronic forms are generally enclosed in a fibrous capsule. Leptomeningitis, usually purulent, and sinus thrombosis are not infrequent concomitants. An abscess of the brain may remain localized and even latent for years, or it may extend rapidly and burst into a ventricle or externally upon the surface of a hemisphere, setting up a terminal meningitis. Pos-

[1] Arch. f. Ohrenk., 1905–1906, lxvii, 1.
[2] Jour. Amer. Med. Assoc., 1920, lxxv, 532.

sibly in rare instances recovery may ensue from inspissation of the pus and shrinking of the membranous capsule.

**Symptoms.**—Abscesses of the brain may be latent or nearly latent for a long time. This is particularly true of those that form slowly, remain small, and affect "silent" areas of the brain. In the majority of cases, however, there are indications of heightened intracranial tension combined with symptoms produced by irritation or destruction of centers or tracts possessing definite functions—the so-called focal symptoms. The usual phenomena of septic infection may also be present, but these are far more frequently due to the primary suppurative process or concomitant lesions, such as diffuse encephalitis, meningitis and sinus thrombosis, than to the abscess itself.

*General Symptoms.*—Headache, more or less severe, is an important symptom. In many cases it is referred to the region of the abscess. Tenderness of the head to percussion is occasionally observed, but it may not be over the abscess. Vomiting is less constant than headache, but it is common, especially in cerebellar abscesses. In the late stages it may be projectile. Sometimes there is distressing vertigo. Choked disc occurs less regularly and is less marked, as a rule, than in tumor of the brain. Generalized convulsions are somewhat infrequent, but may occur whether the motor area is involved or not. In uncomplicated cases, except at the beginning and just before death, the temperature is likely to be normal or subnormal. With increasing intracranial pressure the pulse may become infrequent, although very often it is accelerated throughout. At the onset, especially of acute cases, there may be delirium or marked irritability alternating with apathy; late in the disease stupor develops and gradually deepens into coma. With the increasing drowsiness there is often repeated yawning. Generally emaciation and a sallow, cachectic appearance are striking symptoms in some of the long-standing cases. While leucocytosis is the rule in rapidly developing abscesses, the white-cell count is usually normal in the chronic encapsulated forms. In the absence of meningitis or cortical encephalitis spinal puncture yields negative results.

*Focal Symptoms.*—These are much the same as those of tumor in corresponding situations. An abscess of the *frontal cortex* rarely manifests definite localizing symptoms. Involvement of the *motor area* usually declares itself by Jacksonian spasms and increasing paresis of a monoplegic or, less frequently, of a hemiplegic type. Suppuration in the *temporosphenoidal lobe* frequently results in compression of the adjacent motor area or tracts and, therefore, is likely to cause Jacksonian epilepsy and spastic hemiplegia on the contralateral side, with increase of the knee-jerk and a plantar reflex of the extensor type. In left sided lesions aphasic symptoms are commonly observed. Deafness may also occur, but it usually lacks significance, since the ear itself is so often involved in these cases. In *cerebellar abscess* the most constant signs are occipital headache, vomiting, nuchal stiffness, vertigo, lateral nystagmus, and asynergy or defective coördination. Paresis of the cranial nerves, especially those from the fifth to the twelfth, and contralateral hemiparesis from involvement of the pyramidal tracts are not uncommon.

The course of the disease varies greatly. There are acute cases in which the duration does not exceed a week. In these the onset is stormy and the symptoms continue without intermission until death. In many cases, especially of otitic abscess, three stages are recognizable: the first, comparatively short and marked by irregular fever, headache, mental confusion, vomiting, chilliness and weakness; the second (dormant stage) lasting

months or, exceptionally, years, with few or no symptoms other than those of increased intracranial pressure; and the third (terminal stage) characterized by signs of acute encephalitis or meningitis and resulting in death in a comparatively short time. Again, there are cases in which the onset is insidious, the clinical picture for months that of slight septic infection, with episodic attacks of headache and vomiting, and the terminal feature, stupor passing into coma.

**Diagnosis.**—Abscess of the brain without evidence of pus elsewhere in the body may be extremely difficult to recognize. Even when such evidence is present serious difficulty may arise, since meningitis and sinus thrombosis may produce a similar picture and the association of one or both of these conditions with abscess is not uncommon. Marked irritative symptoms speak in favor of *meningitis*, whereas aphasia and paresis of the limbs are suggestive of abscess. Kernig's sign and rigidity of the neck occur more frequently in meningitis, but are not pathognomonic. The absence of fever is against meningitis, but the presence of fever, of course, does not exclude abscess. The presence of pus cells and of bacteria in the cerebrospinal fluid is indicative of meningitis. The *serous meningitis* of Quincke, which occasionally arises in the course of purulent otitis, may closely simulate abscess, but it is accompanied by greatly increased pressure of the arachnoid fluid and lumbar puncture often results in marked improvement or cure.

Frequent rigors, an irregular high temperature with large oscillations, distention of the superficial veins and bacteriemia point to *sinus thrombosis*. The differential diagnosis of abscess from *tumor of the brain* is considered on p. 958. Occasionally abscess and tumor occur together. Hirschmann[1] has collected 34 such cases. In *extradural abscess* the most obtrusive symptom is headache referred to the side of the lesion, focal signs are usually absent, and the eye-grounds are, as a rule, normal. A profuse discharge of pus from the ear, out of proportion to the capacity of the tympanic cavity, may in some instance arouse suspicion, but it is not decisive, as the same phenomenon occasionally occurs with abscess in the brain substance.

**Prognosis and Treatment.**—As spontaneous recovery in brain abscess is rarely observed, proper treatment of the disease can only be operative. As Collins[2] remarks, "Delaying the operation until the appearance of unequivocal localizing symptoms, or procrastinating by operating on the mastoid when one is reasonably assured that brain abscess exists, is a far greater injustice to the patient than subjecting him to an exploratory trephining." Of 419 cases of abscess collected by Starr[3] recovery occurred in 197 and of 79 cases of sinus thrombosis recovery occurred in 41.

## ACUTE NON-SUPPURATIVE ENCEPHALITIS

**Etiology.**—Acute non-suppurative inflammation of the brain substance, although often present in association with acute leptomeningitis, is comparatively uncommon as an independent affection. It may occur, however, as a complication or sequel of the acute infectious diseases, notably influenza, and according to some writers (Klebs, Leichtenstern), it may in rare instances be the chief expression of meningococcus infection. In some cases of acute

[1] Zeitsch. f. Ohrenh., 1914, lxxi.
[2] Amer. Jour. Med. Sci., April, 1899.
[3] New York Med. Record, Mar., 1906.

poliomyelitis the brain as well as the spinal cord is affected (*acute polioencephalomyelitis*) and occasionally the incidence of this disease appears to be chiefly upon the brain. The *acute polioencephalitis anterior* of Strümpell[1] is now generally conceded to be but a variety of acute poliomyelitis. This writer believed that a large number of infantile cerebral palsies could be traced back to an acute inflammatory process in the cerebral cortex. According to Oppenheim,[2] injury of the head, even without fracture of the skull, favors the occurrence of encephalitis. Many of the cases of non-suppurative inflammation of the brain occurring without any known antecedent infection or traumatism have doubtless been examples of the disease now variously designated *epidemic encephalitis*, *lethargic encephalitis* and *nona*, and which has prevailed somewhat extensively since the pandemic of influenza in 1918. Indeed, it is likely that so-called influenzal encephalitis has often been of this type (see p. 270). Finally, in one form of the disease, the so-called *polioencephalitis superior of Wernicke*, chronic alcoholism appears to be an important factor, although other toxic influences, particularly botulism, may produce a somewhat similar anatomical picture.

**Morbid Anatomy.**—Any part of the brain may be affected. In some cases, as in those first reported by Strümpell, the cortical portion bears the brunt of the attack; in others the gray matter about the third ventricle and aqueduct of Sylvius is the seat of the process (*polioencephalitis superior*); and others again the lesions are chiefly localized in the pons and medulla (*polioencephalitis inferior* or *acute bulbar palsy*). Various pathologic forms of the disease have been described, but the best known is the hemorrhagic type, in which there are hemorrhagic extravasations, single or multiple, together with evidences of destruction of nerve tissue and a varying amount of cellular infiltration. The ultimate result in patients who survive the acute attack may be complete resolution or the formation of patches of sclerosis or, more rarely, small cysts.

**Symptoms.**—The onset is acute but not sudden. In the infectious cases general symptoms consisting of headache, restlessness, vomiting, delirium, and somnolence deepening into stupor are usually present. The temperature is frequently elevated. In the course of a day or two focal symptoms, varying with the location of the lesions, make their appearance. These generally take the form of hemiplegia or monoplegia, although aphasia, conjugate deviation of the eyes, palsy of one or more of the ocular muscles, hemianesthesia, ataxia, and choreiform movements of the limbs also occur. Owing to the gradual increase of the inflammatory lesions, general convulsions or epileptiform seizures of the Jacksonian type often precede the paralysis, and the other local signs develop one by one, more or less irregularly. In *acute polioencephalomyelitis* atrophic paralysis of one or more limbs (acute anterior poliomyelitis) usually forms part of the clinical picture and in *acute polioencephalitis inferior* glosso-labia-laryngeal paralysis of rapid onset is the chief localizing feature. In some instances, as in the cases reported by Taylor, Nonne, Mills and Wilson, Griffith, Reh and others, the cerebellum seems to have been especially affected (*acute cerebellar encephalitis*), pronounced asynergy of the limbs, a drawling or jerky speech, and not rarely nystagmus and tremors or choreiform movements being the outstanding focal manifestations.

The *polioencephalitis superior* of Wernicke, which usually occurs in persons who have passed through one or more attacks of delirium tremens, is characterized by delirium, ataxia of gait and speech, acute ophthalmoplegia,

[1] Jahrb. f. Kinderh., 1885, xxii, 173.
[2] *Die Encephalitis*, Wien, 1907.

tremor of the tongue and hands, optic neuritis, general weakness and stupor. Polyneuritic symptoms are sometimes observed and occasionally epileptiform seizures occur, especially at the onset. Death usually ensues in the course of a few days or weeks, but not rarely the disease terminates in a chronic delirium of the Korsakow type.

**Diagnosis.**—In many cases of acute encephalitis the diagnosis can be made only hypothetically by excluding other possibilities. The disease differs from *acute meningitis* in the absence of hyperesthesia, pronounced stiffness of the neck, retraction of the abdominal wall, general muscular rigidity and characteristic changes in the cerebrospinal fluid, and from *cerebral apoplexy* in the occurrence of delirium, stupor, fever, etc. some time in advance of the paralysis, and in the more gradual development and extension of the paralysis. *Sinus thrombosis* is usually distinguishable by the presence of a focus of suppuration elsewhere, high remittent fever, rigors, distention of superficial veins, etc. *Cerebral abscess* usually arises from traumatism, from purulent diseases of the cranial bones (otitis media) or from suppurative processes in the thoracic cavity, but it may depend upon one of the specific general infections and in this event the differential diagnosis from non-suppurative encephalitis may cause insurmountable difficulties.

**Prognosis and Treatment.**—The outlook is uncertain, but varies with the location and severity of the lesions. Polioencephalitis superior of Wernicke and acute polioencephalitis inferior, irrespective of the cause, are ordinarily fatal. In the epidemic form of encephalitis, in the form following acute infections, and in the encephalic and cerebellar types of acute poliomyelitis the prognosis as to survival is fairly good. Recovery may be complete, but recovery with defects corresponding with the area of destruction is common, especially in children. Mental impairment, paralysis, epileptiform seizures, choreiform movements, an arrest of development, or any combination of these phenomena may remain as sequelæ.

As to **treatment,** the application of cold to the head, local bloodletting over the back of the neck or the temporal region, warm baths, thorough evacuation of the bowels, and, if irritative symptoms are severe, the administration of sedatives, especially bromids, are the measures most likely to prove useful. Local palsy should be treated in the same manner as that resulting from acute poliomyelitis.

## APHASIA

**Definition.**—Aphasia is the partial or complete loss of the power to express thought in language or to comprehend the symbols of language, resulting from changes in the centers for articulatory memories or word conceptions or changes in the association-fibers joining these centers.

**Etiology.**—In the majority of cases aphasia depends upon a destructive lesion of the brain, such as hemorrhage, embolus, thrombus, or tumor affecting the centers of language or the tracts connecting them, which, with few exceptions, are in the left hemisphere in right-handed persons and in the right hemisphere in left-handed persons. The phenomenon is not always due, however, to organic disease, a functional form, usually transitory, sometimes occurs under great excitement, after epileptic seizures, in hysteria, in migraine, and in certain toxic conditions, such as uremia and diabetes.

**Varieties.**—It is customary to speak of two forms of aphasia, the motor and the sensory, although the distinction between the two cannot always be sharply drawn. In the motor form the defect is one of emission and in the sensory form, one of reception.

*Motor aphasia* is a loss of power, partial or complete, to communicate by articulate utterance thought to others, even though the peripheral speech apparatus may be in a condition to functionate. All grades of the disorder are observed from so-called syllable-stumbling to inability to utter more than a few words or even a single word. In some instances the aphasic has command of but one meaningless phrase and this is repeated when ever he attempts to talk. Occasionally, the capacity to express emotion in exclamation is retained while that of intellectual speech is lost.

Two subdivisions of motor aphasia are generally made, according as the lesion destroys the posterior part of the third frontal convolution (Broca's region), in which the conception of movements necessary for speech or the articulatory kinesthetic memories appear to be localized, or as it destroys the fibers that convey motor impulses from this region to the peripheral speech apparatus. The former is known as *cortical motor aphasia* and the latter, as *subcortical motor aphasia*.

In cortical motor aphasia, or Broca's[1] aphasia, the patient is unable to speak spontaneously, to repeat words after some one else, to read aloud or to himself, and to write spontaneously or from dictation. He is able, however, to comprehend articulate speech and to write from copy. In subcortical motor aphasia (aphemia, anarthria) the patient has the capacity to call into existence the motor memory pictures of speech (faculty of internal language), but is unable to externalize them in the form of articulate words. Although he is without power to speak or to read aloud he understands spoken language and is able to read to himself and to write. That the patient is fully aware of the word that he cannot pronounce may be shown by the Proust-Lichtheim test, which consists in indicating by pressure of the hand the number of syllables in the word and the number of letters in each syllable. Hemiplegia usually accompanies the defect of articulation.

*Sensory aphasia*, or *Wernicke's*[2] *aphasia*, consists in an inability to recognize or recall the sound or the appearance of words. It depends upon an injury to the cortex of the temporal or temporoparietal region, or to the auditory or visual pathways beneath this part of the cortex, and, as in the case of motor aphasia, the lesion is usually on the left side. If the auditory verbal memories alone are lost the defect is termed *word-deafness*, and the lesion is usually in the superior temporal convolution, contiguous to the cortical center of hearing; if the visual memories of words are lost, the defect is termed *word-blindness*, and the lesion is traced to the angular gyrus, contiguous to the occipital visual center.

In word-deafness the sense of hearing is intact, but there is a loss of power to comprehend spoken language; in word-blindness, although there may be no loss of visual acuteness, there is inability to comprehend printed or written language. Owing to the proximity of the center for visual memories to the primary visual area, word-blindness is frequently accompanied by right homonymous hemianopsia. A congenital and familial or hereditary form of word-blindness, unaccompanied by hemianopsia, and probably the result of a developmental defect, has been observed by Thomas, Stephenson, Hinshelwood[3] and others.

[1] Bull. de la Soc. Anatomique, 1861.
[2] Der Aphasische Symptomenkomplex, 1874.
[3] Brit. Med. Jour., Mar. 18, 1911.

It is customary to subdivide each of the two varieties of sensory aphasia into cortical and subcortical forms, although the line of distinction in this case is not so clear as it is between cortical and subcortical motor aphasia. In *cortical auditory aphasia* the patient can speak volitionally, but not being able to comprehend his own speech, he is likely to misplace words (paraphasia) or to talk jargon. He cannot understand spoken language nor can he read aloud or write. In *subcortical auditory aphasia,* internal language being intact, spontaneous speech is preserved and the patient can both read and write. In *cortical visual aphasia* the patient cannot read aloud (alexia), nor can he write (agraphia) either spontaneously or from dictation. In *subcortical visual aphasia* the patient can write spontaneously and from dictation, but being unable to understand what he has written he is likely to make many mistakes.

In opposition to the orthodox teaching upon the subject of aphasia, which the foregoing description attempts to portray, Marie[1] maintains that there is no clinical or pathological evidence in support of Broca's doctrine that the third left frontal convolution plays a special part in the function of speech. He attributes all aphasia (intellectual deficit for the comprehension of language) to a lesion of Wernicke's area—gyrus supramarginalis, gyrus angularis, and the posterior part of the gyrus temporalis superior and the gyrus temporalis inferior—which he regards as the speech center, but one that cannot be divided into subcenters for auditory and visual speech. The entire process of language, he insists, is governed by one center and the different disturbances are due to different degrees of injury suffered by that center.

Further, according to Marie, the classic aphasia of Broca is a combination of aphasia (Wernicke's or Marie's) with anarthria (difficulty in articulation), the two lesions responsible for it being in the zone of Wernicke or the white fibers thence and in the lenticular nucleus or its neighborhood respectively. To sum up his teaching, he holds that if we must classify the different forms of the disease they should be grouped as: (1) *Intrinsic aphasia* in which Wernicke's zone or the fibers that come from it are directly affected by the lesion (Broca's and Wernicke's aphasia); (2) *extrinsic aphasia* in which the zone of Wernicke and its fibers are not directly affected, but the lesion is situated in the neighborhood and outside that area, in the lingual and fusiform lobes, giving rise to alexia, or in the lenticular nucleus, causing pure anarthria or the "pure motor aphasia" of some authors.

Moutier,[2] under the auspices of Marie, has collected 27 cases in which the third frontal convolution was alone involved, but in which no aphasia occurred.

**Method of Examination.**—In studying cases of aphasia, Dana[3] suggests that attention should be paid to (1) voluntary speech; (2) exclamatory speech; (3) responsive speech; (4) associative speech, such as counting, saying alphabet, etc.; (5) quality of speech, such paraphasia, confusion, sterotypy, jargon; (6) repeating spoken words; (7) indicating the number of syllables in a word—to show that the patient knows that it is a word; (8) writing; (9) writing to dictation; (10) copying; (11) singing (humming tunes); (12) gesturing; (13) understanding gestures; (14) understanding spoken words, sentences and complex directions; (15) naming things seen, felt, heard, touched, smelled, and tasted; (16) naming abstract things and qualities; (17) recalling to mind objects named; (18) reading understandingly, aloud

[1] La Semaine Médicale, 1906, xxvi.
[2] L'Aphasia de Broca, Paris, 1908.
[3] New York Med. Jour., Aug. 10, 1907.

or silently; (19) reading letters or numerals; (20) reading aloud without understanding; (21) knowledge of the use of things; (22) general intelligence. It should also be ascertained that the patient is not deaf as a result of any lesion of the ear itself and that there is no paralysis of the labial, lingual, or laryngeal muscles.

**Prognosis and Treatment.**—The prognosis depends upon the nature and extent of the lesion and the intelligence of the patient. Age is also an important factor. Children may learn to speak again after extensive damage to the speech centers, whereas small lesions in old persons may produce a lasting aphasia. As a rule better results are obtained in traumatic cases than in those arising from spontaneous hemorrhage or occlusion of the vessels. The *treatment* of aphasia itself consists in reëducating the patient to talk, read, and write after the manner employed in instructing the child.

**Motor Apraxia.**—The term apraxia was originally applied to an inability to recognize the nature or use of familiar objects, but since the publication of Liepmann's[1] studies this defect has been designated *agnosia* and the term apraxia has been applied to inability to make purposive movements or combinations of movements, other than those used in speaking or writing, by one who is neither paralyzed or ataxic. According to this definition, an object is recognized, its use is known, the limbs themselves are readily moved, but purposeful movements of the affected member are lost. Apraxia is usually, although not invariably, an accompaniment of aphasia. It is apparently due to lesions of the left hemisphere involving the corpus callosum or the frontal convolutions anterior to the motor area.

## CEREBRAL PARALYSIS IN CHILDHOOD

Paralysis of cerebral origin in young children usually assumes the form of *hemiplegia* or *diplegia*, the lesion in the first instance being unilateral and in the second instance bilateral. In diplegia one side of the body may be affected much more than the other, or the legs may suffer much more than the arms (*cerebral spastic paraplegia*). Of 225 cases analyzed by Sachs,[2] there was hemiplegia in 156 and diplegia or paraplegia in 69. The cause of the paralysis may be effective before, during or after birth.

In the *prenatal cases* the change found in the brain at necropsy usually consists of a loss of substance in the form of a depression or cavity extending more or less deeply into the hemisphere (porencephaly), agenesis or atrophy of the convolutions of variable extent, or an area of sclerosis. Some disturbance of the cerebral circulation in the fetus, induced, perhaps, by trauma or disease affecting the mother during the pregnancy, is supposed to be the cause of these defects, but our knowledge of the subject is by no means exact. In the *intrapartum cases* the final lesion is usually chronic meningo-encephalitis or sclerotic atrophy of certain lobes or regions of the brain, the result, as a rule, of a meningeal, or rarely intracerebral, hemorrhage, which has been brought on by injury at birth. In the *postnatal cases* there is found in the large majority of cases an area of sclerosis or a cyst, which has had its origin in hemorrhage, thrombosis, embolism or primary acute encephalitis. Even in this last group the paralysis usually appears in the first four years of life. One of the infectious diseases of childhood, especially diphtheria, whooping cough, or measles, is frequently responsible for it. Septic infection of

[1] Monat. f. Psy. u. Neurol., 1905, 1906.
[2] Sachs: Nervous Diseases of Childhood, 1905, 447.

pulmonary or gastrointestinal origin is sometimes the determining factor. Hereditary syphilis may also excite it. Traumatic injury of the skull is an exceptional cause. In a few cases of infantile cerebral paralysis the only demonstrable change in the central nervous system has been an abnormal fineness or paucity of the fibers of the pyramidal tracts (Spiller, Biswanger, Gerlich, Rhein). Prenatal and birth palsies are most often diplegic or paraplegic, while postnatal palsy is commonly hemiplegic.

**Symptoms.** *Spastic Diplegia and Paraplegia (Little's[1] Disease).*—In the *prenatal cases* nothing abnormal may be noticed until the child begins to walk. In many cases, however, the mother's attention is attracted very early to the child's condition by rigidity of the legs, which is manifest whenever an attempt is made to separate them. Occasionally, the tonus of the affected muscles is so exaggerated that the slightest passive movement brings on marked spasm. In the cases that develop *intrapartum*, in association with difficult labor, the increased intracranial pressure is frequently indicated by a tense bulging of the fontanelle, deep asphyxiation, general or unilateral convulsions, and inequality of the pupils. The clinical picture of fully developed cerebral diplegia is usually very characteristic. The lower limbs are rigid, the thighs are adducted, and the feet are often extended in a position of equino-varus. Locomotion is more or less impeded and the gait is spastic. The arms are usually less affected than the legs and may escape entirely. The muscles of the head are not, as a rule, involved, although wry-neck, facial contortion, difficulty in articulation or strabismus is sometimes present. The tendon reflexes are increased and the muscles of the limbs are poorly developed, but marked atrophy, sphincteric disorders, and sensory changes are absent. In very many cases mental deficiency, varying in degree from slight feeble-mindedness to complete idiocy, occurs as a result of imperfect cerebral development. Involuntary movements of a choreiform or an athetotic character are frequently observed in the affected members and in more than half of the cases epilepsy eventually develops. Occasionally all paretic symptoms disappear, leaving the choreiform movement or the epileptic seizures as the only evidence of the cerebral defect. Spratling ascribes 11 per cent. of 1070 cases of epilepsy to this cause.

Variations in the symptoms are not rarely observed. In some instances actual chorea or athetosis is absent, but the spastic paralysis is accompanied by a general ataxia, every effort to carry out exact movements resulting in a profound disturbance of coördination (*ataxic diplegia*). Occasionally, instead of spasticity there is extreme flaccidity of the muscles, with inability to stand or walk, difficulty in articulation or actual mutism and, not infrequently, a certain degree of ataxia (*atonic-astasic type* of Förster[2]). In the few cases that have come to necropsy sclerosis of the frontal lobes was found. Batten[3] has described a form in which the clinical picture is one of pure ataxia of cerebellar character involving the speech, the gait, and various movements of the limbs (*cerebellar type* of *diplegia*). In this type the mental condition is usually good. Finally, Hunt[4] has described an *ataxic type of cerebral birth palsy*, which on theoretic grounds he believes is due to lesions in the cortex of parietal lobes. The motor disorder, which is unassociated with paralysis, spasticity, epilepsy or serious mental defect, is of the nature of spinal ataxia and persists in the recumbent posture.

*Infantile Spastic Hemiplegia.*—Paralysis of cerebral origin in young children very often develops acutely with general or partial convulsions,

[1] Lancet, 1843, i, 318.
[2] Deutsch. Arch. f. klin. Med., 1909, xcviii, H. 1 and 3, S. 216.
[3] Clin. Jour., 1903, xxii, 81.
[4] Amer. Jour. Med. Sci., April, 1918, p. 505.

or with fever, stupor, vomiting and convulsions, as in acute hemorrhagic encephalitis. In other cases it occurs abruptly in apparent health, very much after the manner of apoplexy in the adult, and in other cases still it has an insidious onset, which at times is not unlike that of brain tumor. The hemiplegia is at first flaccid and later spastic. The face may or may not be involved. In the later stages of severe cases the affected members are found to be more or less stunted in growth, cold and cyanotic, and often distorted by contractures. Sensation is usually normal. Choreiform or athetotic movements occur on the paralyzed side in about one-fourth of the cases. Mental deficiency is less common than in cerebral diplegia, but it is of frequent occurrence. Epilepsy with general or Jacksonian seizures is likely to develop even when the intelligence is good.

**Diagnosis.**—Infantile cerebral paralysis must be distinguished from other paralytic and ataxic conditions occurring in childhood. The distinctive features of both *acute spinal paralysis* (*poliomyelitis*) and *peripheral birth palsy* are the rapid occurrence of muscular atrophy, changes in the electrical reaction and loss of tendon reflexes. Both *Friedreich's* ataxia and *hereditary cerebellar* ataxia are familial diseases and, as a rule, develop at a later period of life than cerebral palsy. In the former the knee-jerk is absent and nystagmus, scoliosis, and certain disturbances of sensation are commonly present; in the latter optic atrophy is frequently observed. *Hydrocephalus* may cause spastic palsy, but the changes in the cranium are diagnostic. *Disseminated sclerosis* is rare in early childhood. Of 206 cases analyzed by Frankl-Hochwort[1] only 8 were in the first 10 years.

*Sydenham's chorea with muscular weakness* may be excluded by its occurrence sometime after birth, and by the absence of spasticity and of other signs of damage to the pyramidal tracts. *Progressive lenticular degeneration* bears some resemblances to infantile cerebral palsy, but it is disease of adolescence and youth. *Progressive torsion spasm* of *childhood* is not likely to come into question as it rarely, if ever, occurs before the sixth year, is confined almost exclusively to Russian and Polish Jews, and is not associated with any mental defect or signs of injury to the pyramidal tracts. *Familial spastic paralysis*, due to diffuse sclerosis of the cerebral cortex or to early degeneration of the pyramidal tracts, resembles cerebral birth palsy, but it affects several children of the same parents and is more likely than the latter to be accompanied by nystagmus, optic atrophy, kyphosis, and scoliosis.

Atonic-astasic cases of cerebral palsy may be confused with *amaurotic family idiocy* and with *amyotonia congenita*, but the first of these two conditions is usually seen in Hebrew infants, is often familial, and is marked by blindness with peculiar changes in the optic disc, and in the latter there is no mental deficiency or disturbance of articulation.

**Prognosis.**—The outlook is uncertain, but, on the whole, it is very unfavorable as to complete recovery. In the *dipleqic* and *paraglegic* cases death often occurs soon after birth or in early infancy. Of the survivals the majority suffer from mental impairment, epilepsy, or permanent rigidity of the limbs. However, in the form which occurs in premature or undeveloped infants and which presents little more than spastic paresis of the legs, and in the ataxic varieties described by Batten and Hunt there is a decided tendency to improvement.

*Infantile hemiplegia* is not often fatal, but the prospect for complete recovery is poor. A variable degree of spastic paresis and defective intelligence is very likely to remain, and in more than 50 per cent. of the cases epilepsy supervenes.

[1] Arb. aus der neurol. Inst. au der Wien. Univ., 1903, x, 19.

**Treatment.**—Craniotomy and removal of the clots should be considered in cases developing at birth and presenting signs of increased intracranial pressure. Two of four operations performed by Cushing in 1905 yielded good results, and since that date craniotomy has been done by others with more or less success. Lumbar puncture has also proved useful in some cases. In later cases when there is a history of difficult labor and papilledema and increased pressure of cerebrospinal fluid are present the removal of meningeal cysts offers some hope of relief. Sharpe and Farrell[1] report that of 65 cases so treated, 9 of the patients died after operation, 8 within two years, 19 were unimproved, 4 disappeared from observation, and 25 were much benefited. In any case after the acute symptoms have subsided warm baths, massage and passive movements are indicated to counteract the tendency to contractures. If the latter have already appeared relief may be afforded by orthopedic appliances, tenotomies, or, in selected cases, division of several posterior nerve-roots. When the intelligence is impaired training in a special institution offers the best chance of improving it.

## HYDROCEPHALUS

Hydrocephalus is an excessive accumulation of serous fluid in the ventricles of the brain. It is sometimes referred to as internal hydrocephalus, to distinguish it from an abnormal collection of fluid between the brain and the dura mater, which has been designated external hydrocephalus. The latter is usually observed in association with inhibited development of the brain (*hydrocephalus e vacuo*), hemorrhagic pachymeningitis, or chronic meningoencephalitis, and is comparatively uncommon.

Internal hydrocephalus may be congenital or acquired. The immediate cause of both forms is a disproportion between the secretory activity of the choroid plexus and the absorptive function of the venous channels of the spinal subarachnoid space,[2] the underlying factors being, on the one hand, (1) an obstruction to the outflow of fluid from the ventricles (*obstructive hydrocephalus*), and, on the other, (2) excessive secretion of fluid or defective absorption, in consequence of adhesions in the spinal subarachnoid space or of changes in the composition of the fluid (*communicating hydrocephalus*). Dandy[3] has shown that the usual cause of communicating hydrocephalus, *i.e.*, of that type in which the ventricles are in communication with the subarachnoid space, is the presence of adhesions, which, as a rule, are located in the mesencephalic or pontine cisterna.

In the congenital form, the more remote cause of the disease is often obscure. Intra-uterine meningitis, the result of syphilis, is probably a factor in some cases. Parental alcoholism is also supposed to play a part. A family predisposition is occasionally observed. Acquired hydrocephalus has its principal source in meningitis, especially the menigococcic form. In obstructive hydrocephalus the actual impediment to the natural drainage of the cerebrospinal fluid may be a congenital malformation, a cicatricial stric-

[1] Jour. Amer. Med. Assoc., Sept. 29, 1917.

[2] It is the consensus of opinion that the cerebrospinal fluid is for the most part a secretory product of the choroid plexus. The flow is from the lateral ventricles through the foramina of Monro to the third ventricle, then through the aqueduct of Sylvius to the fourth ventricle, and thence by the median foramen of Magendie and the lateral foramina of Luschka to the spinal subarachnoid space, where the fluid is normally absorbed.

[3] Johns Hopkins Hosp. Bull., 1921, xxxii.

ture, adhesions, a tumor or a cyst. The site of the obstruction is usually at the aqueduct of Sylvius, but it may be at any part of the ventricular system.

**Morbid Anatomy.**—In the congenital form the cranium is large and round, the bones are thin and pressed apart, and the fontanelles are increased in extent. In long-standing cases the gaping sutures and fontanelles may be filled with numerous Wormian bones. Atrophy of the cerebral convolutions and of various projecting ganglia results from the pressure of the fluid, and in some cases the hemispheres are transformed into great sacs with walls only a few millimeters thick. Secondary degeneration of the pyramidal tracts is a common sequel and not rarely other defects, such as cephalocele and spina bifida, coexist. Occasionally, there is also syringomyelia or hydromyelia. Both lateral ventricles are usually distended, but occasionally, as when only one foramen of Monro is occluded, the condition is unilateral. All the ventricles may be involved, but, as a rule, the fourth suffers the least. The contents of the ventricles, normally about 20 or 30 c.c., may be increased to several hundred or even to several thousand c.c. The fluid is usually clear and watery.

In hydrocephalus acquired after the bones of the skull have become thoroughly ossified and the fontanelles and sutures definitely closed, the head may show little, or no, increase in size. As the cranium can no longer yield, however, the effect of the pressure of the fluid on the brain is much more pronounced than in the congenital form.

**Symptoms.**—In *congenital hydrocephalus* enlargement of the head is usually the first conspicuous symptom. This may be obvious at birth and interfere with the delivery of the child, or it may not attract attention until several months of extrauterine life have passed. In extreme cases a circumference of 100 cm. or more may ultimately be attained. The head is roughly globular with protruding forehead and large tense fontanelles. The scalp is stretched and thin, the hair is sparse, and the superficial veins are dilated. The comparatively small face also presents a peculiar aspect. Owing to the tenseness of the pericranial tissues the eyebrows are elevated and owing to the flattening of the orbital roofs the eyes are prominent and directed downward. In some cases the head becomes so heavy that it cannot be held erect. Strabismus and nystagmus are common symptoms and impairment of vision not rarely occurs from pressure upon the optic tracts or nerves.

Mental weakness ranging in degree from slight feeble-mindedness to complete idiocy is almost always present. Headache is often severe and in young children may be evinced by restlessness and moaning cries. Convulsions occur in a large proportion of cases and may be among the earliest symptoms of the disease. Vomiting is sometimes excited by motion of the head. Spastic paralysis of the limbs, especially the legs, frequently ensues in consequence of injury to the motor tracts. The general nutrition is usually more or less affected, most hydrocephalic children being puny and undeveloped.

The *duration* of the disease is variable. The large majority of patients perish at birth or within a few months after birth. In some instances, however, life is prolonged to puberty or even to old age. Death usually occurs in coma or convulsions or through some intercurrent affection. Occasionally the process is arrested at a comparatively early period and the patient survives with a large head but with normal or fairly good intelligence.

The symptoms of hydrocephalus acquired after the first two years of life are often equivocal. Even after closure of the sutures and fontanelles,

however, some separation of the bones and enlargement of the head may occur, but never to the same extent as in infants. In the majority of cases the symptoms are principally those of increased intracranial pressure, namely, headache, impairment of vision from optic neuritis, dulling of the intellect, vomiting, and paresis of the cranial nerves. Rigidity of the legs frequently supervenes, and eventually the picture may be that of spastic diplegia (Little's disease). Remissions and exacerbations at intervals are often observed. Extreme emaciation is sometimes noted, especially in hydrocephalus occurring with cerebrospinal meningitis. In cases developing after closure of the sutures a sharp, high-pitched clear note, instead of the normal low-pitched non-resonant one, may be heard when the stethoscope is placed over the forehead and percussion is practised over the parietal region (Macewen's sign). The subarachnoid fluid is usually abundant and under increased pressure when communication with the ventricles is free and scanty and under low pressure when such communication is interrupted.

**Diagnosis.**—In congenital hydrocephalus the diagnosis is usually not difficult. In *rickets* the shape of the head is square, the fontanelles are not tense, the intelligence is good, and other signs of the disease are present. In *oxycephaly* the head is elongated antero-posteriorly, the forehead is excessively high (thurmschädel or steeple-shaped skull), optic atrophy appears early, there is often an "adenoid facial expression," the intelligence is unimpaired, and the *x*-ray picture is characteristic ("lordose basillaire"), the middle fossa being on almost the same level as the posterior fossa, the sella turcica, indented and deepened, and the wings of the sphenoid flattened out.

The diagnosis of acquired hydrocephalus, in the absence of an acute onset with meningeal symptoms, may be difficult. The resemblance to *tumor* of the brain, especially of the cerebellum, may be close (Bramwell, Spiller, Finkelberg, Cushing and others). A gradual onset without obvious cause, ataxia of movement, and choked disc are in favor of tumor. The phenolsulphonephthalein tests, elaborated by Dandy and Blackfan[1] and Frazier and Peet,[2] afford a reliable means of distinguishing between obstructive and communicating hydrocephalus. In the obstructive type the absorption of the dye from the subarachnoid space and its excretion by the kidneys are virtually normal, but when the dye is injected into the lateral ventricle it does not appear in fluid withdrawn by lumbar puncture until after the lapse of from 15 to 60 minutes (normal time 5 to 8 minutes). On the other hand, in communicating hydrocephalus the dye passes from the ventricles into the spinal subarachnoid within the normal time, but absorption and excretion by the kidneys is much retarded. Occasionally no phenolsuphonephthalein reaches the urine in four or six hours. Normally from 30 to 60 per cent. should be excreted in the urine within the first two hours. According to Dandy, obliteration of the mesencephalic cisterna which is chiefly responsible for communicating hydrocephalus, can also be demonstrated by cerebral pneumography after air has been injected into the spinal canal.

**Treatment.**—This is still unsatisfactory. If there is evidence of syphilis mercury and iodid may occasionally lead to a cure. Ventricular puncture followed by injection of antimeningitic serum has been successful in some cases of hydrocephalus resulting from cerebrospinal fever. In cases of communicating hydrocephalus dependent upon hypersecretion thyroid extract is worthy of trial, as this drug lessens the secretory activity of the choroid plexus (Frazier and Peet). When the outlets of the ventricles are

[1] Amer. Jour. Dis. Child., 1914, viii.
[2] Amer. Jour. Physiol., 1914, xxxv.

unoccluded spinal puncture, frequently repeated, may be of benefit, transitory or lasting, according to the nature of the pathologic process. On the other hand, lumbar puncture will not afford even temporary relief if communication between the ventricles and subarachnoid space is obstructed. In this case repeated tappings through the fontanelles may be tried, but it is not likely to prove successful; moreover, the operation is sometimes followed by an inflammatory reaction and an exacerbation of symptoms. Apparently the most effective method of dealing with obstructive hydrocephalus is puncture of the corpus callosum, this operation providing an outlet for pent-up fluid into the subarachnoid space, where it may be absorbed.

## PROGRESSIVE LENTICULAR DEGENERATION

(Wilson's Disease)

This is a comparatively rare disease characterized anatomically by bilateral degeneration of the corpus striatum and cirrhosis of the liver, and clinically by tremor, dysarthria, dysphagia, spasticity, contractures, various psychic disturbances and progressive weakness and emaciation. It was recognized vaguely by Frerichs in 1854 and more clearly by Gowers in 1888, but it was first completely described, both clinically and pathologically, by S. A. K. Wilson[1] in 1912.

Progressive lenticular degeneration is a disease of adolescence and youth, and affects the two sexes about equally. It is very often familial, but it is not known to be hereditary or congenital. It has been suggested that the basic etiologic factor is a toxin having a selective action on the corpus striatum, but whether this toxin arises in the cirrhotic liver or is a common cause of both lesions can only be conjectured. Syphilis is without etiologic influence.

**Pathologically,** the essential findings are bilateral degeneration of the corpus striatum and cirrhosis of the liver. The striate changes involve both the neostriatum (caudate nucleus and putamen) and the paleostriatum (globus pallidus) and vary from discoloration and sponginess to extensive excavation. Microscopically, there is destruction of the parenchymatous tissue with more or less gliosis. The adjacent pyramidal tracts are rarely involved. Cirrhosis of the liver of a mixed type, partly multilobular and partly monolobular, is invariably present. The organ may be enlarged or diminished in size. The spleen is usually enlarged.

**Symptoms.**—The onset is gradual and usually with tremor, which is increased by excitement and by voluntary effort. Hypertonicity, or spasticity, soon appears in the limbs and in the course of time involves all the voluntary muscles, except those of the eyes. The muscular stiffness gives rise to dysarthia or anarthria, to dysphagia, and finally to contractures, with the limbs mainly in a position of flexion. The reflexes, although sometimes difficult to obtain owing to the muscular stiffness, are not definitely altered. Sensory symptoms are absent. The facial expression is usually stupid or actually idiotic, and in the majority of cases mental disturbance, especially emotionalism with varying degrees of dementia, sooner or later develops. As the disease progresses muscular weakness and emaciation also supervene and eventually the patient becomes bedridden and helpless. As a rule, there are no symptoms referable to the cirrhosis of the liver,

[1] Brain, 1912, xxxiv, 295.

although exceptionally digestive disorders, icterus and even ascites may be observed. The illness invariably progresses to a fatal issue, the course being relatively acute or chronic. Acute cases, which are frequently marked by an irregular fever and cachexia, terminate within a few months; chronic cases, with motor symptoms only, last from two to seven years.

Progressive lenticular degeneration must be distinguished from paralysis agitans, disseminated sclerosis, pseudosclerosis and progressive torsion spasm. *Paralysis agitans* occurs at a later period of life and has a longer course. Moreover, in this disease the tremor tends to subside during action and is not accompanied by any pronounced malposition of the extremities. *Disseminated sclerosis* rarely begins in childhood and is characterized by a scanning speech, nystagmus, optic atrophy and symptoms indicating involvement of the pyramidal tracts, such as Babinski's sign and exaggeration of the tendon reflexes. It is doubtful whether lenticular degeneration can be distinguished with certainty from *pseudosclerosis*, but in the latter, as contrasted with the former, there is sometimes a peculiar brownish discoloration of the skin or pigmentation of the cornea, and according to Strümpell,[1] the tremor is more conspicuous than the spasticity. *Progressive torsion spasm*[2] is also characterized by hypertonicity and choreiform movements or tremors, but in this disease, which occurs almost exclusively in Russian or Polish Jews, the motor disability affects chiefly the lower extremities and trunk, some of the muscle groups are often hypotonic, the spasm is of a twisting and tractile quality, articulation is not involved and the intelligence is normal.

The **treatment** of progressive lenticular degeneration is merely palliative.

## GENERAL PARESIS

**(General Paralysis of the Insane; Paretic Dementia; Dementia Paralytica; Cerebral Tabes; Chronic Meningoencephalitis)**

**Definition.**—General paresis is a chronic disease of the brain characterized anatomically by degeneration of the cortical neurons, and clinically by a progressive loss of mental and physical power. That general paresis and locomotor ataxia are but different localizations of the same morbid process, one affecting the brain and the other the spinal cord, is now generally conceded. Not infrequently the two diseases are combined, or succeed one another, in the same individual.

**Etiology.**—Antecedent syphilitic infection is the essential etiologic factor, the disease being produced by the spirochæta pallida itself and not, as was formerly believed, by a toxin only indirectly connected with the syphilitic virus. Other factors, such as mental strain, cranial injury, chronic lead poisoning, alcoholism and sexual excesses, may act as coöperative or contributory causes, but none of these apart from syphilis can induce paresis. Indeed, alcoholic and sexual excesses, upon which much stress has been laid, are often evidences of existing mental disorder rather than predisposing factors. General paresis is much more prevalent among people advanced in civilization than among primitive races, but the assertion that the latter are entirely free from it has been shown to be unfounded. Excluding the juvenile type, which depends upon inherited lues, the disease occurs most commonly between the ages of 35 and 50 years and on an average of from 10 to

[1] Deutsch. Arch. f. Nervenh., 1914, l, 455.

[2] A full description of this disease is given by J. R. Hunt, Jour. Amer. Med. Assoc., Nov. 11, 1916.

15 years after the syphilitic infection. Men are attacked much more frequently than women, the disproportion between the two sexes being especially marked in the large cities and among the higher classes. Townspeople furnish many more cases than those who live in the country. A neuropathic inheritance seems to have some influence, but undoubtedly its importance has been exaggerated.

**Morbid Anatomy.**—The dura mater is usually thickened and in places adherent to the skull. Hemorrhagic pachymeningitis is a frequent finding. The pia mater is thickened, opaque and in places adherent to the cortex. The sulci and the areolar spaces beneath the pia, where the latter is free, contain an excess of fluid, which may be clear or turbid. The convolutions are shrunken and the sulci abnormally wide. The cortex is usually anemic and indurated, although in cases of very short duration it may be hyperemic and softened. All of these changes are most marked in the fronto-parietal regions. The ventricles are dilated and contain an excess of fluid, and the ependyma, especially of the fourth ventricle, is often thickened and granular.

Microscopically, the most pronounced changes are found in the meninges and in the cerebral cortex, especially that of the frontal region. The meninges are thickened and infiltrated with mononuclear lymphocytes and plasma cells. The lamellæ of the cortex are disarranged. The ganglion cells show various stages of degeneration, many being completely destroyed. The tangential fibers and collaterals are also reduced in number. The walls of the blood-vessels are thickened and the perivascular spaces are irregularly dilated and filled with lymphocytes and plasma cells ("mantle infiltration"). A loss of cells and fibers is also foundi n the pons, medulla and cerebellum, and the spinal cord usually shows areas of degeneration in the posterior columns and pyramidal tract. The peculiar feature of the process is the great destruction of parenchymatous tissue, but whether the primary lesion is a degeneration of the neurons themselves or an interstitial process with secondary atrophy of the nerve-elements is still a debatable question.

**Symptoms.** *Prodromal Stage.*—The onset of general paresis is so insidious that the earliest stage often escapes recognition. Forgetfulness, especially for recent events, difficulty in fixing the attention, defective judgment, irritability and transient states of emotional depression are usually among the first symptoms to attract attention, but they are likely to be ascribed to neurasthenia. Gradually, the patient's disposition changes; he becomes careless in business matters, indifferent to relatives and friends, neglectful of the proprieties, intemperate in eating and drinking, extremely egotistical, easily excited to anger or violence, untidy in appearance, absurdly extravagant and parsimonious by turns, and often untruthful, erotic and indecent. Not rarely the commission of some crime, for which there is no adequate motive, first directs attention to the patient's true condition.

Somatic symptoms may precede the mental phenomena, but usually they appear simultaneously or later. Among the first to be noted are dull headache, insomnia, neuralgic pains, signs of vasomotor instability (alternate pallor and redness of the face, flashes of heat, etc.), and, still more significant, hesitancy and monotony of speech, transient aphasia, awkwardness of movement (well shown in handwriting), tremulousness of the tongue and lips, abnormalities of the pupils (myosis, mydriasis, inequality, irregularity of contour, sluggish reaction to light), and alteration of the knee-jerk (exaggeration or abolition). Loss of endurance, contrasting strongly with a fictitious sense of well being and great strength, is also an early indication. Finally, at any time, even in the initial period, there may be recurrent attacks of an epileptic or apoplectic nature. It is characteristic

of the paretic that whatever his infirmity he does not complain of it or regard it seriously. Indeed, in many cases he does not even recognize it.

The blood serum yields a positive Wassermann reaction in more than 85 per cent. of the cases and the spinal fluid in at least 95 per cent. Equally important, the spinal fluid regularly shows lymphocytosis (20 to 80 cells), increase of globulin, and a typical colloidal gold reaction.

*Second Stage.*—In this stage the mental failure and disturbances of innervation become pronounced and delusions usually make their appearance. The latter, are, as a rule, of the grandiose type, improbable, and poorly systematized. The patient may conceive that he is engaged in some vast enterprise, that he is fabulously rich, that he has the strength of Hercules, or that he is related to the Deity. Dominated by these ideas, he is inclined to be restless, noisy, and boastful, although self-satisfied and contented, even under restraint. Occasionally the mental exaltation attains to the degree of maniacal delirium. In other cases instead of elation there is pronounced emotional depression with delusions of persecution or of physical illness.

Delusions, however, are not always present. Occasionally there is merely progressive dementia with unusual euphoria or, less frequently, hypochondriacal depression.

The somatic symptoms of the prodromal period are intensified in this stage. The speech is slow, thick and stammering, owing to ataxia of the vocal organs, mental confusion, and, in some instances, actual aphasia. Lapses of words or syllables and repetition of words are especially common and suggestive. Fine tremors are usually apparent, not only in lips and tongue, but also in the hands. The expression is stolid, the pupillary changes of the early stage are more conspicuous, and further, the pupils in many instances no longer respond at all to light, although they still react to accommodation. This reflex iridoplegia, or Argyll-Robertson phenomenon, is very significant, since it is rarely seen except in general paresis and tabes dorsalis. Occasionally the pupils are irresponsive to accommodation as well as to light. Paresis of the external ocular muscles, usually temporary, is often observed. Optic atrophy is also fairly common, especially in tabo-paresis. The gait may be either ataxic or spastic, and the knee-jerk diminished or exaggerated, according as the spinal lesions are more marked in the posterior columns or in the pyramidal tracts. Cutaneous sensibility to touch, pain and temperature is usually more or less impaired, and sooner or later the special senses also suffer. Epileptiform seizures of varying degrees of severity or apoplectiform attacks, followed in some instances by temporary hemiplegia or aphasia, are prone to occur at intervals.

*Third Stage*—In this stage intellectual power is reduced to the point of extinction. The grandiose or melancholy delusions and the emotional state corresponding to them gradually disappear and the patient becomes childish, insensible to his surroundings and frequently filthy in his habits. A marked advance also takes place in the physical deterioration. Locomotion and articulation grow more and more difficult, emaciation sets in, the bladder and rectum become unretentive, the patient becomes bedridden and helpless, and at last contractures of the arms and legs make their appearance and bedsores form over parts subjected to pressure. Other trophic lesions, such as abnormal brittleness of the bones, arthropathies, perforating ulcers of the feet, hematomata of the ears and other parts, are also observed at times in the later stages of the disease.

**Tabo-Paresis.**—The term tabo-paresis is applied to those cases which present the conspicuous features of both general paresis and tabes dorsalis.

The tabetic symptoms may precede or follow the mental disturbances or both groups of phenomena may develop at about the same time.

**Juvenile General Paresis.**—General paresis before the age of 20 is rare, although it is more common than juvenile tabes. In nearly all cases the sufferer has been the victim of hereditary lues. In 10 of 69 cases analyzed by Bechet[1] one of the parents had also suffered from general paresis. The mental condition is usually one of simple dementia; grandiose delusions are uncommon; epileptform attacks are of frequent occurrence; remissions are lacking and the duration is comparatively long.

**Diagnosis.**—The differential diagnosis between general paresis, and *diffuse interstitial cerebral syphilis* is sometimes impossible, especially at an early period of the disease. However, a history of recent specific infection (within 3 or 4 years), severe nocturnal headaches, coarse paralysis, particularly if complete, early optic neuritis, recurring somnolent or semi-comatose states, and an irregular evolution proceeding by fits and starts point to cerebral syphilis; while tremor of the lips and tongue, extreme miosis, a typical Argyll-Robertson pupil, a drawling hesitating speech, ataxic movements, and uniform mental enfeeblement, with euphoria, a loss of the autocritical faculty, a profound change in character and personality are equally suggestive of paresis.

*Alcoholic pseudoparesis* resembles paretic dementia, but in the former terrifying hallucinations, especially of sight, outbreaks of delirium, and complete disorientation are common, the mental state, at least for a time, is one of stupidity and confusion rather than of actual dementia, the Argyll-Robertson pupil is almost never seen, and the spinal fluid is negative as regards lymphocytosis, antibody reaction, and globulin excess. Neurasthenic symptoms are often conspicuous in paretic dementia, but *primary neurasthenia* nearly always begins in early adult life, and while it is characterized by ready mental and physical fatigue, it does not impair the judgment and autocritical faculty of the patient, alter his character or personality, affect his speech, produce pupillary anomalies or cause cytologic or chemical changes in the cerebrospinal fluid.

**Prognosis.**—The outlook is virtually hopeless, and the average duration of the disease does not exceed 3 or 4 years. In many cases, however, remissions lasting from several months to a year or longer are observed. Death may be due to a cerebral seizure or to some intercurrent affection, such as septicemia, pyelonephritis, pneumonia, or tuberculosis.

**Treatment.**—This includes the avoidance of all mental and physical excitement and the employment of the general measures recommended in cases of neurasthenia. Owing to the difficulty of distinguishing clearly between coarse cerebral syphilis and paretic dementia and to the fact that in the latter the destructive lesions are frequently accompanied by an actual exudative syphilitic process, vigorous treatment with arsphenamin, preferably according to the method of Swift and Ellis, and with mercury should be instituted. Such sedatives as bromids, scopolamin, paraldehyde and trional may be required from time to time to allay mental excitement. For obvious reasons the treatment is best carried out in a well-ordered asylum or sanatorium.

[1] These de Paris, 1897.

# SYSTEMIC DISEASES OF THE SPINAL CORD

## TABES DORSALIS

(Locomotor Ataxia; Posterior Sclerosis)

**Definition.**—The term tabes dorsalis is used to designate a progressive degeneration of the ascending sensory neurons, involving the posterior columns of the spinal cord, the posterior nerve-roots, and frequently certain cranial nerves, especially the optic nerve.

The disease was termed locomotor ataxia (Duchenne) because its most striking symptom is a loss of the power of coördinating muscular movements and posterior sclerosis because its most conspicuous anatomical feature is sclerosis of the posterior columns of the spinal cord.

**Etiology.**—Fournier, in 1876, first drew attention to the close relationship of syphilis to tabes dorsalis and at the present time it is generally accepted that the latter cannot develop without the existence of the former. Definite evidence of luetic infection is obtainable in nearly all cases. The disease usually develops in from 8 to 12 years after the appearance of the chancre, but it may occur as early as the second or third year or as late as the thirtieth. The percentage of cases of syphilis which are followed by tabes is not known, but it is small, probably less than 5 per cent. It is a common observation that in patients with syphilis who are destined to develop specific lesions of the nervous system the early manifestations of the infection are usually mild. Whether the factor which determines involvement of the spinal cord or brain is infection with a special strain of spirochætæ having a neurotoxic action, or is an inherent lack of resistance in the nerve tissues themselves, or is a sensitization of these tissues by a small quantity of virus, which for a time remains dormant and is later called into activity, is uncertain. Owing to the peculiar character of the lesions in tabes dorsalis and paretic dementia and the failure of antiluetic remedies to produce any decided impression on them, it was formerly believed that these diseases were due to a toxin only indirectly connected with syphilis and hence they were spoken of as parasyphilitic (Fournier) or metasyphilitic (Moebius) manifestations. But the findings in the cerebrospinal fluid and the demonstration of spirochetes in the spinal cord of tabetics and in the cerebral cortex of paretics have made the theory of indirect action untenable and have proved conclusively that in each case the immediate cause of the morbid process is the syphilitic virus itself.

Overexertion, sexual excesses, exposure to cold, nervous strain, and the immoderate use of alcohol may properly be regarded as auxiliary or coöperative causes of tabes, for while such factors are without power to produce the disease in the absence of antecedent syphilis, they may favor its occurrence by making the nervous system more vulnerable to the action of the specific virus. Traumatic tabes is also mentioned, but the evidence in its favor cannot be considered as conclusive. It is certain, however, that injury may aggravate the disease and excite characteristic pains in the part affected. Excluding the rare juvenile form, which is almost always traceable to congenital syphilis, tabes dorsalis occurs most commonly between the ages of 30 and 50 years. Men are attacked much more frequently than women. The disease is far more prevalent among peoples advanced in civilization than among primitive races. It was formerly rare in the American Negro, but at present it is not uncommon.

**Morbid Anatomy and Pathogenesis.**—In advanced cases certain changes in the spinal cord and posterior nerve-roots are usually apparent to the naked eye. Thus, it may be observed that the pia arachnoid between the posterior roots is cloudy, thickened, and adherent to the cord, that the posterior roots themselves are thinner and more translucent than normal, and that the posterior columns are shrunken, of a grayish color, and firmer than the rest of the cord. Except in the comparatively rare cases known as tabes superior, in which the disease begins in the cervical cord, the changes are usually most conspicuous in the lumbar or lumbo-dorsal region.

The microscopic appearances vary with the stage of the process and the number of neurons affected. In early typical cases a section of the lumbar cord usually exhibits a small area of degeneration in each of Burdach's columns near the posterior horn. These areas correspond to Pierret's "bandelettes externes," from which are given off the reflex collaterals to the anterior horns and the fibers to the columns of Clark. In cases of longer duration the areas of degeneration are more extensive and involve the columns of Goll (funiculus gracilus), as well as those of Burdach (funiculus cuneatus); and in advanced cases all of the posterior columns, including the tracts of Lissauer (faciculus dorsolateralis), may be occupied by overgrown neuroglia tissue, except the cornu commissural zone and the oval fields of Flechsig, which consist of fibers (endogenous) arising from cells within the cord itself. Section of the dorsal cord may show degeneration of Goll's columns alone, if only the long fibers from the lumbosacral region are affected, or of both Goll's and Burdach's columns if the dorsal roots are also implicated. In the areas involved the myelin sheaths and axis cylinders, in greater or less numbers, are found to have disappeared and to have been replaced by proliferated glia. Some thickening of the walls of the bloodvessels may also be seen, and in cases not too far advanced there is usually present a more or less pronounced perivascular lymphocytic infiltration in the posterior columns themselves and in the pia, especially in the latter.

The spinal cord, however, is not the only part of the nervous system affected. Similar degenerative changes are observed in the posterior roots, in the sensory roots of certain cranial nerves, and to a less extent in the spinal root ganglia and the peripheral sensory nerves. In some instances the neurons of the cerebral cortex also share in the destructive process, the condition under these circumstances being really one of combined tabes and general paresis, or of so-called tabo-paresis.

The **pathogenesis** of tabes has been much discussed. While it seems to have been fairly well established that the disease is an ascending degeneration of the sensory neurons secondary to a destructive lesion of the posterior nerve-roots, opinion is sharply divided as to whether the nerve-roots are primarily attacked by the syphilitic toxin or whether, as Nageotte has maintained, there is first a subacute inflammation of the pia over the posterior surface of the cord which causes compression and eventually destruction of the entering roots. However produced, the tabetic change is peculiar in consisting chiefly of a destruction of the parenchymatous tissue, that is, of the ganglion cells and fibers, whereas in so-called simple cerebrospinal syphilis the change involves principally the vascular interstitial tissue and is essentially one of inflammatory exudation. Clinically, it is sometimes difficult to distinguish between these two processes, and even anatomically it is not always possible to divide them sharply.

As the columns of Goll and Burdach containing the long ascending branches of the dorsal root fibers, which transmit afferent impulses (proprioceptive impulses) from the muscles, joints and tendons toward the brain,

are especially involved in tabes, it will be readily understood why impairment of motor coördination, sense of position, muscular tonus, deep sensibility, etc. (bathyanesthesia) should be a conspicuous feature of the disease, while sensations of touch, heat, cold, etc. (exteroceptive impulses), which reach the brain through more or less isolated paths, are less affected.

**Symptoms.**—In accordance with general custom three stages of tabes may be recognized, if it be understood that these stages are merely artificial divisions and that the symptoms do not invariably appear in the order indicated. Symptoms which are usually late in developing are in some cases the first to reveal the existence of the disease.

*The Initial or Preataxic Stage.*—Disturbances of sensation are among the earliest manifestations. Patients complain of tingling, numbness, formication and other *paresthesias* in various parts of the body, especially in the feet and legs and about the trunk. One of the most suggestive of these paresthetic phenomena is the so-called *girdle sensation*, which consists in an unpleasant feeling of constriction about the waist, as though a cord were being drawn tightly around it. A sense of fatigue or even of exhaustion out of all proportion to the effort put forth is also referred to in many instances. Of all the sensory disturbances, the most important and distressing to the patient are the so-called *lightning pains*. These occur in about 90 per cent. of the cases and in the majority are the first symptom perceived. At times they antedate the other phenomena by years. They are felt most frequently in the legs and not rarely they are so violent that the patient screams aloud. The attacks, which occur at varying intervals, usually last but a few seconds. In some instances the pain is accompanied by exquisite tenderness of the skin in the region affected and exceptionally it is followed by an outbreak of petechiæ or of herpes. Like the pains of so-called rheumatism or sciatica, with which they are sometimes confused, tabetic pains are much influenced by changes of weather. Overexertion and emotional excitement are also likely to induce them.

Closely related to the lancinating pains, but much less frequent, are the so-called *visceral "crises."* These may occur at any period of the disease, even at the onset. The most common are the gastric crises, which usually consist of paroxysms of abdominal pain with vomiting, appearing suddenly, continuing for several hours or even days, and then ceasing as abruptly as they came. Analysis of the gastric secretion frequently, but not invariably, shows an increase in acidity, and accompanying the pain there is sometimes pronounced arterial hypertension. Hematemesis is occasionally observed. In some cases the pain is slight or absent and incessant vomiting alone occurs and in other instances the crisis is represented by paroxysmal gastro-succorrhea. In the intervals between the attacks, which vary in length from a few days to several months, the digestive functions are usually normal.

Laryngeal crises are occasionally observed. These consist of paroxysms of severe cough, with stertor, dyspnea, cyanosis, and sometimes temporary loss of consciousness. Intestinal, rectal, vesical, clitoral, renal and ocular crises also occur, but are rare. Apart from the lancinating pains and the crises, tabetics occasionally suffer from attacks of migraine or of ordinary neuralgia.

The sensibility of the muscles and of the deeper tissues generally is always impaired. This may be shown by a loss of vibratory sense (*pallanesthesia*) and by analgesia of the tendons and nerve-trunks when pinched, of the bones when percussed, and of the eyeballs and testicles when compressed. To this source must also be ascribed the *Romberg sign*, which consists in an inability to stand without unduly swaying when the eyes are

shut and the feet are close together. This phenomenon is very constant and usually appears early, long before actual ataxia. Another evidence of impairment of deep sensation is the patient's inability to recognize the position of his limbs or their relation to one another when his eyes are closed. In the later stages of the disease stereognostic perception may also be disturbed.

Objective disturbances of the sensation of touch, heat, cold and pain are common and may appear early in the disease. Zones of *tactile anesthesia* or of *analgesia*, having a segmentary arrangement, are found in many cases about the chest (tabetic cuirass), on the inner surface of the arms and forearms, in the perineal region, and on the outer aspect of the legs and thighs. Hyperesthesia or hyperalgesia may be found at the borders of the anesthetic zones or independently in plaques. Many tabetics are unduly susceptible to cold or hot water. Perception of pain stimuli is often considerably retarded and in some cases a single pin-prick is felt in several places (polyesthesia) or is even referred to the opposite side of the body (allochiria). One of the earliest and most constant indications of tabes is weakening or *loss of the tendon reflexes*, particularly of the knee-jerk (Westphal's sign). It is noted in about 95 of the cases, and is dependent upon interference with the conduction of afferent impulses through the posterior roots in the lumbar region. Of course, if the lesions are limited to the upper segments of the cord the knee-jerks may be unimpaired. The tendo-achilles reflex usually disappears coincidently with that of the patellar tendon. The superficial reflexes often remain intact until a late period.

For the same reason that the knee-jerk is weakened or abolished there is also a lack of muscular tonus (*hypotonia*). Normally, this is maintained by continuous slight discharges of motor energy emanating from the anterior horn cells of the cord and called forth by centripetal sensory stimuli. In tabes the anterior horn cells, although intact, are largely cut off from peripheral impulses, especially from those which should reach them through the afferent muscle nerves, and as a result these cells are unable to transmit to the muscles the energy requisite for normal tonus. The hypotonia thus brought about is often manifested, even early in the disease, by the ease with which passive movements of unusual extent may be performed and the great range of flexion and extension that may be produced at various joints.

*Paralysis of the ocular muscles*, often transitory in the beginning, and manifested by diplopia, ptosis, strabismus, etc., occurs in a large proportion of the cases. The third nerve is most frequently involved, less often the sixth, and rarely the fourth. Pupillary anomalies are also extremely common. Myosis is the rule, but occasionally there is mydriasis. More significant still, is reflex iridoplegia (rigidity of the pupil to light) with normal reaction to accommodation. This sign, the *Argyll-Robertson phenomenon*, is present in about 80 per cent. of all cases.[1] In some instances it is confined to one side and rarely it is for a time intermittent. The site of the lesion responsible for the Argyll-Robertson pupil is not definitely known, but it has been placed by some authors in the fibers which pass from the proximal end of the optic nerve to the oculomotor nuclei. Increasing impairment of visual acuity from *primary atrophy* (*gray or white atrophy*) *of the optic nerve* occurs in about 20 per cent. of the cases, and is sometimes the first indication of the disease. It is a remarkable fact, one for which there is yet no satisfactory

[1] The Argyll-Robertson pupil is very strong evidence of syphilis of the central nervous system, especially of tabes or general paresis, but it is not absolutely pathognomonic of this condition, as in rare instances it has been observed also in syringomyelia (Déjérine and Mirallee), in alcoholism (Nonne), in trauma (Vincent) and in tumor involving the corpora quadrigemina (Buzzard).

explanation, that when amaurosis is an early symptom ataxia and some of the other tabetic phenomena may be late in appearing or may not appear at all. Indeed, with increasing blindness symptoms that have already developed, notably the fulgerant pains, frequently become less marked. Nevertheless, optic atrophy is of serious import, inasmuch as it is often a forerunner of mental deterioration.

Cranial nerves other than those terminating in the eye, such as the auditory, olfactory and facial, are occasionally affected.

*Urinary disturbances*, especially difficulty in emptying the bladder, is observed in the preataxic stage almost as frequently as the lancinating pains. Constipation is the rule, and loss of expulsive power in the rectum is not an unusual symptom. Satyriasis is sometimes noted in the beginning of tabes, but as the disease progresses the sexual appetite usually becomes impaired and eventually there is often complete impotence.

In the active stage of tabes the *cerebrospinal fluid* usually shows a lymphocytosis (20–60 cells), an increase of globulin, a positive Wassermann reaction (70–80 per cent. of the cases), and a partial colloidal gold reaction.

*Ataxic Stage.*—As the disease advances *ataxia*, or imperfect coördination of muscular action, gradually develops. This is first shown, as a rule, in the legs, and for a time may be apparent only when the patient attempts to move about in the dark. Sooner or later, however, walking becomes unsteady even in bright daylight. With marked ataxia the gait is characteristic. The patient stands with the head bent forward, the legs widely separated, and the eyes fixed on the floor. In stepping out he raises the feet abnormally high, throws them out loosely, and brings them down abruptly with a stamp, the heels often striking the floor first. On turning quickly he sways backward and forward, and sometimes falls in his effort to regain proper balance. After a time, he can walk only by the help of canes and at last locomotion becomes wholly impossible. In the recumbent position the ataxia is well shown in movements of the legs requiring the coördinate action of a number of muscles, such as touching the knee with the heel of the opposite foot, especially if such movements be made without any aid from the sense of sight. Ataxia of the upper extremities is less constant. It may be recognized in writing, sewing, buttoning the clothes, etc., or by such tests as bringing the tips of the index fingers together from a distance when the eyes are closed or touching the tip of the nose with the tip of the index finger after the arms are widely separated. The main cause of the ataxia is disturbance of the muscular sense.

Notwithstanding the marked incoördination of movements, there is usually little or no impairment of coarse muscular power in the extremities until near the close of the disease. Occasionally, however, actual paresis of the legs supervenes as a result of concomitant degeneration of the anterior horn cells or of peripheral neuritis.

Trophic phenomena occur with considerable frequency, but are usually late in appearing. The most important is the so-called *arthropathy*, which was first described by Charcot[1] in 1868. This remarkable lesion is observed in from 3 to 6 per cent. of the cases. Clinically it is manifested by the sudden appearance of a firm, painless swelling of a joint, extending to the adjacent soft parts, and followed by changes in the articular surfaces leading to subluxation or dislocation. Pathologically, the condition resembles somewhat arthritis deformans. The knee is affected in about half of the cases, and next in order follow the hip-joint, tarsus, shoulder, elbow and ankle. The wrist, the finger and toe joints are seldom involved. Frank[2]

[1] Arch. de Physiol. Norm. et Path., Paris, 1868, No. 1.

[2] Centralbl. f. d. Grenzgebiete der Med. u. Chir., 1904, vii, 17.

has collected 26 cases of tabetic arthropathy of the spine. It is important not to mistake for a true arthropathy the common retroflexion of the knee which results from imperfect tendinous support and relaxation of the ligaments.

*Abnormal fragility of the bones* often occurs in tabes and as a result fractures, usually painless, are sometimes produced by insignificant force. Both arthropathies and painless fractures are apparently more common in women than in men. Herpes, pemphigus and falling out of the hair and of the nails are occasionally observed. *Perforating ulcer of the foot* is not uncommon. It usually appears on the plantar surface of the great toe or ball of the foot. Torpid ulceration of the nasal septum or of the hard palate, atrophy of the alveolar processes with falling out of the teeth, and necrosis of the terminal phalanges have been described. Atrophy of certain muscles, such as those of the legs and feet, of the hands, or of the tongue (hemiatrophy) sometimes supervenes. According to Déjérine it occurs in 20 per cent. of the cases. It is probably always an incidental condition due to concomitant degeneration of anterior horn cells or to peripheral neuritis. The general nutrition of tabetics also suffers, and in the later stages of the disease most of them become pale and emaciated.

Except in cases of combined tabes and general paresis (tabo-paresis), in which mental symptoms are, of course, a conspicuous feature, the mind is usually unaffected, although some degree of apathy or depression may develop.

*Paralytic Stage.*—The tabetic may be said to have entered upon the third or paralytic stage when the ataxia has become so pronounced as to confine him almost wholly to his chair or bed. In this helpless state he may linger for years. Death is almost always the result of some secondary or intercurrent affection, such as cystitis, pyelonephritis, septicemia from bedsores, pneumonia, colitis, cerebral apoplexy or tuberculosis. In rare instances it has been due to a laryngeal or gastric crisis or to bulbar paralysis.

**Variations and Associations.**—Variations from the usual type are not rare. Occasionally the disease develops early in life, between the ages of 5 and 25. This so-called *juvenile type* of tabes is almost invariably the result of hereditary syphilis. Urinary disturbances and amblyopia from optic atrophy are usually among its earliest manifestations. Crises are common, but ataxia is, as a rule, slight and late in appearing. In *tabes superior* the symptoms begin in the upper extremities and bulbar phenomena usually develop early. *Sacral tabes* has also been described. In some instances tabes is represented by only a few symptoms and the condition remains stationary for a long time or even throughout (*rudimentary* or *abortive tabes*), and very rarely cases are observed in which there is only one really conspicuous manifestation (*monosymptomatic tabes*).

Other diseases often occur in association with tabes. A combination with peripheral neuritis, with progressive spinal muscular atrophy, and even with interstitial spinal syphilis (Binswanger, Sträussler, Alzheimer, Jakobs) is occasionally observed, but the most frequent concomitant disease of the nervous system is general paresis (tabo-paresis). Late syphilitic lesions of the aorta (mesarteritis, aneurysm, aortic insufficiency) are common associations. Aortic aneurysm was found in 19 of 100 cases by Lesser,[1] in 3 of 34 cases by Burr[2] and in 3 of 113 female tabetics by Mendel and Tobias.[3] The last authors also describe 4 cases of tabes complicated with

[1] Berlin. klin. Woch., Jan. 24, 1905.
[2] Jour. Nerv. and Ment. Dis., Mar., 1912.
[3] Die Tabes der Frauen, Berlin, S. Karger, 1912.

paralysis agitans. Barkan[1] cites 8 cases of combined tabes and exophthalmic goitre and similar cases have been reported by P. Marie, Barie, Moebius, Charcot and others.

Childbirth proceeds normally in tabetic women, with the exception that it is almost entirely painless.

**Course.**—The course of tabes is usually very slow, often extending over two or three decades. The preataxic stage lasts, as a rule, three or four years, but it may be considerably longer; and the ataxic stage is frequently protracted to 15 or 20 years. Acute cases, however, are occasionally observed in which the paralytic stage is reached in two or three years. The disease is usually progressive, but not always so. Thus, when atrophy of the optic nerve is an early feature, the motor symptoms may be late in appearing or may not develop at all, and rarely even when the optic nerve is not affected the disease does not advance beyond the rudimentary stage. Spontaneous remissions not rarely occur and marked improvement sometimes follows appropriate treatment, but it is doubtful whether actual recovery has ever been observed. Reports of cure must be regarded with considerable skepticism, owing to the impossibility at times of differentiating clinically between tabes and interstitial spinal syphilis.

**Diagnosis.**—The diagnosis of well-developed tabes is not usually difficult. The lancinating pains, the loss of the knee-jerk, the Argyll-Robertson pupil, Romberg's sign, the girdle sense, the ataxia, the bladder disturbances, the optic atrophy, and the lymphocytosis of and the positive Wassermann reaction with the spinal fluid are the most constant and significant symptoms.

*Cerebellar disease* sometimes simulates tabes, but the gait of the former differs from that of the latter in being of a more swaying character like that of a drunken person, moreover, in cerebellar disease the tendon reflexes are usually exaggerated; occipital headache, vertigo, choked-disc and vomiting are frequently observed; while lancinating pains, Argyll-Robertson pupil, girdle sense, and Romberg's sign are wanting. *Multiple neuritis*, especially the alcoholic form, may be mistaken for tabes when the ataxia is conspicuous and the loss of muscular power is slight (pseudo-tabes or neurotabes peripherica of Déjérine). Loss of knee-jerk, muscular incoördination, Romberg's sign, and disturbances of sensation are the symptoms common to both conditions. In neuritis, however, the ataxia develops more rapidly than is usually the case in tabes, the special etiologic factor can, as a rule, be demonstrated, the pains are more persistent, there is almost invariably well-marked paresis (footdrop), and the nerve-trunks are frequently tender; and, on the other hand, bladder disturbances, lymphocytosis of the spinal fluid, and, in the large majority of cases, reflex pupillary rigidity are absent.

*Friedreich's ataxia* produces in common with tabes loss of knee-jerk and motor incoördination, but it may be differentiated by the family history, by the presence of nystagmus, a peculiar speech, and characteristic deformity of the feet, and by the absence of pupillary changes, sphincteric disturbances, and lightning pains. *Interstitial syphilis of the spinal cord* often bears a close resemblance to tabes. The early appearance of the symptoms after infection, an irregular anomalous course, the occurrence of motor paralysis (except of the ocular muscles), especially if asymmetrical and transitory, of optic neuritis or choked-disc and of a great increase in the lymphocytes of the spinal fluid are suggestive of interstitial syphilis; while contrariwise a typical Argyll-Robertson pupil, disturbance of the bladder, complete absence of reflexes, and so-called primary atrophy of the optic nerve are in favor of tabes.

[1] Boston Med. and Surg. Jour., June 18, 1914.

*Subacute combined sclerosis of the spinal cord*, which is most frequently observed as an accompaniment of pernicious anemia, presents many of the features of tabes and may come into question if it develops before the characteristic blood changes appear, but it may be distinguished by the absence of reflex iridoplegia and lancinating pains, by the presence of retinal hemorrhages rather than optic atrophy, and in many cases by the occurrence of Babinski's sign and exaggerated knee-jerk. Gastric crises are not likely to be confused with *organic abdominal conditions* if all of the symptoms are carefully analyzed; nevertheless, Nuzum[1] found that in 1000 cases of locomotor ataxia no less than 97 unnecessary operations had been performed for supposed cholelithiasis, peptic ulcer, appendicitis, salpingitis, etc.

**Treatment.** *General Measures.*—Rest, both physical and mental, is of vital importance. Erb advises that the patient should live as if he were an old man, quietly, regularly, and with no excitements. In some cases it is advisable to begin the treatment with complete rest in bed for a week or two. The diet should be non-stimulating and easily digestible. Alcohol and tobacco should be used sparingly, if at all. Sexual excess is exceedingly injurious. Every precaution should be taken to avoid exposure to cold and wet, and, if feasible, the patient should spend the winter months in a warm equable climate. Tepid baths of 80°–85° F. are sometimes of service, but very hot baths and cold baths are usually harmful. Many natural springs have been recommended, the most popular being the Hot Springs of Arkansas, those of Virginia, and those of Los Vegas, New Mexico, in this country, and the thermal baths at Rehme, Nauheim, and Aix-la-Chapelle in Europe. Patients in whom the disease is far advanced should, of course, be spared the expense and discomforts attendant upon a long journey .

The systematic practice of coördinated movements, as originally recommended by Frenkel, is often successful in lessening the ataxia, the improvement sometimes lasting for years. Even in advanced cases this method of treatment is worthy of trial. If good results are to be secured, however, it must be conducted by a skillful attendant and regularly supervised by the physician himself. If left to the patient it is more likely to prove harmful than beneficial. The exercises are contraindicated when the pains are of frequent occurrence, when there is advanced arterial disease, when there are severe arthropathies, and when there is a tendency to spontaneous fractures. For the details of the "reëducation method" the reader is referred to Frenkel's monograph on the treatment of ataxia. Massage is sometimes of value in that it affords a means of securing some of the benefits of exercise without the expenditure of energy.

*Drugs.*—In recent cases antisyphilitic remedies should be given a thorough trial, more especially because of the difficulty in determining with certainty whether a case is one of true tabes or of exudative interstitial syphilis of the cord. Even in true tabes, however, some improvement may occur. Courses of arsenic, in the form of arsphenamin, should be given preferably by the method of Swift and Ellis. According to this method the patient is given intravenously about once a week or once in two weeks 0.3–0.6 gm. of arsphenamin, and after 30 to 60 minutes is bled to the extent of 50 mils of blood. The serum is then separated from the blood and inactivated at a temperature of 132.8° F. (56° C.) for 30 minutes, and within 24 hours a dose of 20 to 25 mils of undiluted serum or 30 mils of 50 per cent. serum with normal salt solution is introduced by gravity into the spinal canal after an equal amount of cerebrospinal fluid has been removed. The patient should remain in bed 24 or 48 hours after the treatment. In addition to arsphenamin, mercury

[1] Jour. Amer. Med. Assoc., Feb. 12, 1916.

should be administered by inunction or by hypodermic injection, and an iodid by the mouth. In some cases tonics are also indicated.

*Treatment of Special Symptoms.*—When the pains are severe the most potent remedial measure is absolute rest in bed. Light touches of the actual cautery or sinapisms over the root of the nerve supplying the affected part occasionally afford relief. Deep massage is sometimes of service. Mitchell has found the alternate application of ice and hot water useful. Flannel bandages applied firmly from the toes up to the middle third of the thigh sometimes do good. A snugly fitting abdominal binder may also be used to lessen girdle pain. Electricity, in the form of the faradic brush, static spark, or stabile galvanic anode, is worthy of a trial.

The most generally useful anodynes are acetphenetidin, antipyrin and the salicylic compounds. According to Osler, the prolonged use of nitroglycerin, given in increasing doses until the physiologic effect is produced, is of great service in allaying pains and diminishing the frequency of crises in all cases of tabes in which there is increased arterial tension. In some cases drainage of the spinal canal is effective. Eventually, recourse must be had to morphin, but its use should be deferred as long as possible.

Gastric crises may require withholding of food by the mouth for a time, the patient being sustained by nutritive enemas. Lavage is often beneficial. The application of sinapisms over the epigastrium may do good. Morphin hypodermically is sometimes necessary. In refractory cases resection of the posterior roots of the seventh to the tenth dorsal nerves may produce satisfactory results. Numbness and paresthesia sometimes yield for a time to local applications of faradism given with the wire brush. Vesical weakness should receive the most careful attention. The bladder must be thoroughly emptied, if need be by catheterization. On the first appearance of cystitis the bladder should be thoroughly washed out with weak antiseptic solutions.

## FRIEDREICH'S ATAXIA

(Family or Hereditary Ataxia)

**Definition.**—Friedreich's ataxia is a chronic disease of rare occurrence appearing in several members of one family or generation and characterized by sclerosis of the posterior and lateral columns of the spinal cord, degeneration of spino-cerebellar tracts, and occasionally atrophy or agenesis of the cerebellum itself.

**Etiology.**—The disease is essentially familial, although sporadic cases are sometimes observed. Of 145 cases collected by Griffith[1] in 1888 all occurred in 79 families. In one family 8 children were affected. Only exceptionally, is a history of direct transmission from one generation to another obtainable and therefore the term hereditary ataxia suggested by Friedereich[2] is scarcely appropriate. The disease usually develops between the ages of 6 and 14 years, but occasionally it appears earlier or later in life. The sexes are about equally affected. Alcoholism and a neuropathic tendency in the ancestors are mentioned as possible etiologic factors. Not infrequently the first signs have followed closely on one of the specific fevers.

**Morbid Anatomy.**—The lesions vary considerably in extent. As a rule, the spinal cord appears abnormally small and the pia is somewhat

[1] Trans. Col. of Physicians, Phila., 1888.

[2] Bericht d. Versamm. Deutsch. Naturforsch u. Aerzte zu Speyer, 1861.

thickened, especially between the posterior roots. Sclerotic changes are found in the columns of Goll and Burdach, the crossed pyramidal tracts, the direct cerebellar tracts, and frequently the tracts of Gowers and the columns of Clarke. The posterior roots may be affected too, and occasionally the degeneration may be traced into the medulla. The form of family ataxia which Marie[1] associated with primary degeneration of the cerebellum and which he designated as *hereditary cerebellar ataxia* is probably not a distinct affection, but only a variety of Friedreich's ataxia, for since Marie published his paper in 1893 most of the necropsies that have been made in cases such as he described have shown no changes in the cerebellum but merely atrophy of the spino-cerebellar tracts, and, moreover, cases have been described which clinically were intermediate between the ataxia of Friedreich and that of Marie.

The **pathogenesis** of family ataxia requires further elucidation, but it is probable that as a result of congenital inferiority the nerve-elements in the affected portions of the central nervous system prematurely undergo degeneration and eventually are replaced by an overgrowth of neuroglia.

**Symptoms.**—The disease ordinarily begins with disturbance of coördination in the muscles of the lower extremities. Slight at first, the awkwardness of movement gradually increases until finally, after the lapse of several years, locomotion becomes impossible. In attempting to walk the patient staggers and reels like a drunken person, the ataxia being cerebellar in type rather than tabetic. Romberg's sign is present in the majority of cases. The knee-jerk is usually abolished, but Babinski's phenomenon can frequently be elicited. As the ataxia increases muscular contractures and certain deformities, especially talipes varus or equinovarus, with extension of the great toes, commonly appear. Curvature of the spine (kyphoscoliosis) also develops in many instances. In the course of time the incoördination attacks the muscles of the upper extremities and eventually the patient becomes utterly helpless. Actual paralysis, however, is not often observed except in the final stage of the disease. The articulation is almost always affected. It is slow and indistinct and at times explosive. Nystagmus, evoked by rapidly turning the eyes several times from side to side, is extremely common, and not rarely tremors or choreiform movements are also noted. The patient's expression is usually dull, but his intelligence is often up to the average. The appreciation of touch, pain and temperature is only slightly affected, but the sense of position and the recognition of vibration, of double contacts and of shape are usually much disturbed (Saunders[2]). The pupillary reflexes are intact and only exceptionally is there any disturbance of the sphincters. The disease is progressive and incurable, but it may last 20 or even 30 years. Death is usually the result of some intercurrent affection.

In *Marie's form* (hereditary cerebellar ataxia) the symptoms appear, as a rule, after puberty, the knee-jerk is exaggerated, atrophy of the optic nerve and paresis of the ocular muscles are common, and there is little tendency to scoliosis or club-foot.

**Diagnosis.**—Friedreich's ataxia may readily be distinguished from *juvenile tabes* by its familial character, by the occurrence of nystagmus, of alterations in speech, and of deformities of the feet and spine, and by the absence of sphincteric disturbance, of the Argyll-Robertson pupil and of crises. The differentiation of *multiple sclerosis* from Marie's cerebellar ataxia is less easy, although a careful analysis of the symptoms will usually lead to a correct decision. The former usually begins with spastic paresis,

[1] La semaine médicale, 1893, xiii, 444.
[2] Brain, 1914, xxxvi, No. 2.

the latter with ataxia. In multiple sclerosis, also, the tremor is more constant and pronounced and is of the intention type, the speech is syllabic or staccato rather than slurring, apoplectiform attacks are common, and there is little tendency to family occurrence. Between multiple sclerosis and Friedreich's ataxia there is less resemblance. In favor of the former are exaggeration of the knee-jerk, spastic paresis, and changes in the optic nerve.

*Gross disease of the cerebellum* is not likely to offer any special difficulty in diagnosis, as it is nearly always marked by symptoms of increased intracranial pressure, such as headache, vomiting, convulsions, and choked disc.

## PROGRESSIVE INTERSTITIAL HYPERTROPHIC NEURITIS OF INFANTS

This rare affection, first described by Déjérine and Sottas in 1893, is definitely familial and develops in early childhood. It presents the usual symptoms of tabes dorsalis in combination with atrophy of the muscles, especially in the distal parts of the limbs, and a characteristic thickening of the peripheral nerves. The facial muscles are frequently involved and, as a rule, kyphoscoliosis is also present. The disease resembles *progressive neural muscular atrophy* (Charcot-Marie-Tooth form of muscular atrophy), which is also familial, but in the latter tabetic phenomena, thickening of the peripheral nerves and kyphoscoliosis do not occur.

## AMYOTROPHIC LATERAL SCLEROSIS

**Definition.**—Amyotrophic lateral sclerosis is a comparatively rare disease characterized anatomically by degenerative atrophy of the pyramidal tracts and the cell bodies of the lower motor neurons in the spinal cord, medulla and pons, and manifested clinically by paresis, muscular atrophy, spastic phenomena, and symptoms of bulbar paralysis.

**Etiology.**—Very little is definitely known regarding the etiology of the disease. Syphilis is probably a factor in some cases. Traumatism and overexertion have been mentioned as possible causes. In the majority of cases the symptoms first appear between the ages of 25 and 50. Males are somewhat more frequently affected than females. A familial tendency is occasionally observed.

**Morbid Anatomy.**—The chief lesions are (1) sclerotic wasting of the pyramidal tracts, both crossed and direct; (2) atrophy of the ganglion cells in the anterior horns of the spinal cord; and (3) atrophy of the motor nuclei of the cerebral nerves in the medulla oblongata and pons. The peripheral motor nerves related to the affected cell bodies and the muscles innervated by these nerves also present degenerative changes. The lesions are usually most marked in the cervical and upper dorsal segments of the spinal cord, but long stretches of the motor paths in both directions are often affected, and occasionally the entire motor central nervous system from the cerebral cortex to the lowest cord-levels is involved.

**Symptoms.**—In the majority of cases the disease begins like progressive muscular atrophy of the Duchenne-Aran type, weakness and wasting gradually developing in the small muscles of the hands and in a variable time spreading to the muscles of the arms, shoulders, neck and trunk. As

the disability increases, contracture makes its appearance, and in consequence of this change the arms are drawn toward the body, the forearms are pronated, and the fingers are thrown into a claw-like position. The lower extremities are usually affected sometime after the upper, and in them there is likely to be marked spasticity with the paresis, but comparatively little atrophy. Indeed, when the disease first shows itself in the legs the clinical picture for months may be precisely that of primary lateral sclerosis, as originally described by Erb. Occasionally the symptoms are confined for a time to one side of the body (descending or ascending hemiplegic type), an upper or, more rarely, a lower extremity being first attacked and a little later the other member of the same side becoming affected.

The tendon reflexes all over the body are exaggerated, clonus is readily demonstrable, especially in the feet, and Babinski's sign, or extension of the great toe upon irritation of the sole of the foot, is nearly always present. The atrophying muscles are the seat of fibrillary twitching and when tested electrically show diminished irritability or even reaction of degeneration. A feeling of fatigue or soreness is sometimes experienced in the affected members, but otherwise sensation is permanently normal. The functions of the bladder and rectum are almost never disturbed.

Symptoms referable to involvement of the nuclei of origin of several motor cerebral nerves in the medulla and pons, such as difficulty in articulation (dysarthria) in chewing (dysmasesia), in swallowing (dysphagia) and in puckering the mouth and protruding the tongue, dribbling of saliva, wasting and rigidity of the muscles in the lower half of the face, etc., appear sooner or later in nearly all cases, and not rarely are the first to attract attention. In upward of 50 per cent. of 100 cases analyzed by Collins[1] symptoms of bulbar paralysis developed within the first year.

It is evident, therefore, that the order of appearance and the preponderance of the individual symptoms vary in different cases according as the changes in the pyramidal tracts or in the motor nuclei are the first to develop or are more marked in one field than in the other, and according as the loss of nuclei occurs first or is more extensive in the medulla or in the spinal cord; thus, *every gradation is observed between amyotrophic lateral sclerosis and primary lateral sclerosis, between amyotrophic lateral sclerosis and pure spinal progressive muscular atrophy,* and *between amyotrophic lateral sclerosis and chronic progressive bulbar paralysis.*

**Course.**—Amyotrophic lateral sclerosis is always fatal, death being due, as a rule, to some pulmonary complication, such as deglutition pneumonia. The course is shorter than that of pure progressive spinal muscular atrophy, seldom extending over more than 3 or 4 years. In 18 cases studied by Raymond and Cestan[2] the average duration was 28 months.

**Diagnosis.**—Amyotrophic lateral sclerosis may be differentiated from *pure progressive spinal muscular atrophy* by the accompanying spastic phenomena (rigidity, exaggerated reflexes, clonus, etc.), and from *myelitis* by the absence of sensory changes and sphincteric disturbances. The occurrence of muscular atrophy and of bulbar symptoms will usually serve to distinguish the disease from *pure primary lateral sclerosis,* but when these manifestations are late in appearing and spastic paresis is the dominant feature the difficulty in diagnosis may be for the time insurmountable. Confusion with *syringomyelia* or *chronic hypertrophic pachymengitis* is not likely to occur owing to the presence of dissociated disturbances of sensation in the former and of local pains in the latter.

[1] Amer. Jour. Med. Sci., June, 1903.
[2] Rev. Neurologique, 1905.

**Treatment.**—This is unsatisfactory. Rest, warm baths, and massage should be tried, although nothing more than slight temporary benefit has ever resulted from the use of these measures. If there is clear evidence of syphilis antiluetic treatment is indicated.

## PRIMARY LATERAL SCLEROSIS

**Definition.**—The term primary lateral sclerosis is used to designate a degeneration of the pyramidal tracts occurring independently of any other lesion and manifested clinically by slowly increasing spasticity and paresis, especially in the muscles of the legs.

As a morbid entity the disease is rare, degeneration of the distal portions of the pyramidal tracts being nearly always secondary to a lesion in the brain or one higher up in the spinal cord, or else a part of amyotrophic lateral sclerosis, disseminated sclerosis, or syphilitic meningo-myelitis. The causes of a purely lateral-tract system sclerosis are somewhat obscure. In a certain proportion of cases syphilis is apparently a factor. One type of the disease is hereditary and familial, and this at least seems to depend upon an abiotrophy, or an inherent lack of vitality in the motor-fibers, which predisposes them to early decay.

**Symptoms.**—The disease begins with a feeling of fatigue, weakness and stiffness in the lower extremities. Not rarely one limb is affected before the other. The loss of power and spasticity slowly increase and at last locomotion becomes extremely difficult or impossible. When the process is well developed the gait is characteristic. The legs are advanced slowly and stiffly, the toes cling to the floor, and the knees, owing to spasm of the femoral adductors, tend to overlap. In the later stages so pronounced is the hypertonia that convulsive tremblings or clonic spasms are excited by every attempt at walking. The tendon reflexes are invariably much increased and ankle clonus and Babinski's sign are readily produced. There are no sensory symptoms, sphincteric disorders, trophic disturbances, or changes in the electric contractility of the muscles. The upper extremities may ultimately share in the spastic paresis, but often they escape entirely. In the hereditary type contractures of the feet are frequently observed.

**Diagnosis.**—This cannot usually be made with absolute certainty for the same clinical picture is at times produced by disseminated sclerosis, amyotrophic lateral sclerosis, subacute combined sclerosis, incomplete transverse myelitis, syphilitic meningoencephalitis, spinal tumor, spondylitis, and cerebral spastic paraplegia, although in the majority of cases these affections present certain features which distinguish them from primary pure lateral sclerosis. *Disseminated sclerosis*, for instance, is usually associated with nystagmus, pallor of the optic discs, scanning speech, and intention tremor. *Amyotrophic lateral sclerosis* is accompanied sooner or later by muscular atrophy, fibrillary twitching, changes in electric excitability and in the final stages by symptoms of bulbar paralysis. In *subacute combined sclerosis* ataxia and disturbances of both superficial and deep sensibility are likely to be present from the beginning, and anemia with irregular pyrexia is often noted. In *transverse myelitis* there are sensory changes, disturbances of the sphincters, trophic phenomena, etc. In *spinal tumor* there are usually, but not invariably, lancinating root pains and objective disturbances of sensation, and definite information is sometimes afforded by roentgenography and by examination of the cerebrospinal fluid. *Syphilitic meningo-*

*myelitis* usually presents a picture of mild or partial transverse myelitis. Sensory phenomena and sphincteric disturbance are commonly observed, the spastic phenomena are less pronounced, as a rule, than those of lateral sclerosis and often show marked variations in intensity from time to time, and, in addition, pupillary changes are frequently noted. *Spondylitis* is only exceptionally unattended by pains and local physical signs. *Cerebral spastic paraplegia* is occasionally familial, but in contrast with hereditary spinal spastic paraplegia it is almost invariably associated with symptoms referable to involvement of the brain, such as mental deficiency, speech disturbances, epilepsy, athetoid or choreiform movements, and palsy of the cranial nerves.

The spastic paraparesis that occasionally develops in old age as a result of *sclerosis of the cerebrospinal vessels* is not likely to be confused with primary lateral sclerosis as it is usually attended with symptoms suggestive of foci of disease in parts of the cord other than the pyramidal tracts, with thickening of the accessible arteries, and with the usual signs of senility. *Hysteria* may rarely give rise to confusion, but the sudden appearance of the symptoms after emotion, the rapid changes in their intensity under suggestion, the absence of Babinski's reflex, and the presence of other hysterical stigmata are usually sufficient for a correct diagnosis.

**Prognosis.**—The disease is incurable, but it usually lasts for years or decades. Death results from intercurrent disease.

**Treatment.**—Little is to be expected from medication. Occasionally, however, a case that appears to be one of pure lateral sclerosis is benefited by antiluetic treatment. For the spasticity warm baths and massage are advisable. Division of a number of the posterior lumbar roots may also afford relief and is worthy of trial if the spasms are very severe.

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## SUBACUTE COMBINED SCLEROSIS OF THE SPINAL CORD

**(Posterolateral Sclerosis; Progressive Spastic Ataxia)**

This is a degenerative process affecting the white matter of the spinal cord, and involving simultaneously or consecutively the posterior and the lateral columns. Isolated foci of degeneration appear in one or the other of the white funiculi and by confluence and secondary degeneration eventually result in continuous paths of sclerosis extending in the posterior columns from the lower thoracic or lumbar region upward and in the lateral columns from the cervical region downward. The gray substance is usually intact. Sharply defined areas of degeneration may also occur in the brain. It is probable that the "ataxic paraplegia" described by Gowers in 1886 included cases of this condition.

Combined sclerosis occurs in a large proportion of cases of pernicious anemia, a toxic factor doubtless being responsible for both the nervous lesions and the blood changes. Occasionally, the symptoms referable to the degenerative process in the spinal cord antedate the onset of the anemia. The disease may also develop in the course of other anemias, leukemia, diabetes, pellagra, certain poisonings (ergot, arsenic) and acute infections. A familial form, apparently dependent upon an inherent weakness (abiotrophy) in the sensory and motor neurons of the spinal cord, has also been reported.

The **symptoms** are those of tabes and spastic paraplegia, variously combined. When the posterior funiculi are chiefly affected the most striking

symptoms are paresthesia, impairment of deep sensation, especially of vibration and joint sensibility (bathyanesthesia), ataxia, hypotony, diminution or loss of the knee-jerk and disturbance of the vesical sphincter, and the only symptoms pointing to changes in the pyramidal tracts may be slight paresis and a positive Babinski's sign. On the other hand, when the pyramidal tracts suffer the greater damage, spastic paraparesis hypertonicity, and exaggeration of the reflexes are the conspicuous features and the only tabetic indications may be paresthesia, impairment of deep sensibility and slight ataxia. Symptoms referable to involvement of the cranial nerves (impairment of taste, hearing, smell, etc.) and various mental disturbances are sometimes noted. Even when the tabetic features are well developed, lancinating pains, crises, pupillary anomalies, changes in the optic nerve or arthropathies rarely appear.

In the differential diagnosis, *disseminated sclerosis* may be distinguished by the intention tremor, staccato speech, nystagmus, and optic atrophy, and *Friedreich's ataxia* by the early onset, choreiform movements, nystagmus, ataxic speech, club-foot and scoliosis. *Syphilis of the spinal cord* may be excluded by the absence of changes in the cerebrospinal fluid, and *cerebellar tumor* by the absence of occipital headache, vomiting, choked disc, retraction of the head, and ataxia of the cerebellar type.

The outlook depends somewhat upon the primary systemic disease, but on the whole it is very unfavorable. However, the condition usually persists for a number of years and rarely of itself causes death. Stationary periods are common and even improvement is sometimes observed. Rest and medication directed to the primary condition are indicated in the treatment. Intravenous injections of arsphenamin have occasionally proved beneficial.

## PROGRESSIVE SPINAL MUSCULAR ATROPHY (CHRONIC ANTERIOR POLIOMYELITIS)

**Definition.**—Progressive spinal muscular atrophy is a chronic disease characterized anatomically by degeneration of the cells in the anterior horns of the spinal cord and manifested clinically by gradual wasting of the muscles with loss of power. It is a rare affection, many of the supposed cases on record being in reality examples of amyotrophic lateral sclerosis, progressive muscular dystrophy or syringomyelia. A distinction is sometimes made between progressive spinal muscular atrophy and chronic anterior poliomyelitis, but this is confessedly fine and some authors refuse to recognize it at all.

**Etiology.**—The etiology is frequently obscure. Excepting the hereditary and familial form occurring in early childhood (Werdnig-Hoffmann type), the disease usually begins between the ages of 25 and 50. Males are more frequently attacked than females. Syphilis is undoubtedly responsible for some cases. The acute infectious diseases and trauma have also been mentioned as causes. The development of progressive spinal muscular atrophy in later life upon the foundation of an acute poliomyelitis that has occurred in childhood has not rarely been noted. Kraumheimer[1] has collected from the literature 50 cases of this kind. Severe muscular exertion may determine to some extent the localization of the symptoms and also hasten the progress of the disease.

[1] Zeitschrift f. Kind., May, 1920.

**Morbid Anatomy.**—Microscopic examination of the spinal cord reveals atrophy or complete disappearance of the ganglion cells in the anterior cornua, especially in the cervical and upper dorsal segments. The affected horns are reduced in size and show an abnormally dense neuroglia. Thickening of the bloodvessels is frequently seen and occasionally there is more or less perivascular round-cell infiltration. Slight degeneration of the pyramidal tracts may also be found, and therefore no sharp line of destruction can be drawn between spinal progressive muscular atrophy and amyotrophic lateral sclerosis. The anterior roots proceeding from the affected ganglion cells and the corresponding muscles always present varying degrees of atrophy.

**Symptoms.**—*Duchenne-Aran-Type.*—The disease develops insidiously and usually first shows itself in the small muscles of the hand. The interossei and the muscles forming the thenar and hypothenar eminences become softer than normal and gradually waste. In most cases the right hand is affected before the left. With the atrophy there is a corresponding loss of muscular power. When the interossei are no longer able to oppose the long extensors and flexors of the fingers, the hand assumes a claw-like form—*main en griffe*—with the first phalanges hyperextended and the second and third flexed. In the course of time, the wasting and paresis spread to the muscles of the forearm, arm, and shoulder,. then to the muscles of the neck and trunk, and still later to the muscles of the lower extremities. At last the patient may be reduced to a mere skeleton. In a few instances the muscles of the legs or those of the shoulder girth have been the first to show the alterations. The muscles supplied by the bulbar nerves usually escape, progressive glosso-labio-laryngeal paralysis being almost always a part of amyotrophic lateral sclerosis. The sphincters are not involved.

The affected muscles remain flaccid and show electric changes varying from diminished irritability to reaction of degeneration, or even complete loss of response to either current. Fibrillary tremors are usually present at some stage or other and the tendon reflexes are decreased or abolished. There is occasionally complaint of coldness or of aching in the wasted members, but otherwise sensation is normal.

*Chronic Anterior Poliomyelitis.*—The features which are supposed to separate this affection from spinal amyotrophy of the Duchenne-Aran type are a subacute onset, the appearance of the symptoms first, as a rule, in the lower extremities, the domination of paralysis over atrophy, the involvement of groups of muscles or of individual muscles *en masse* rather than progressively fiber by fiber, a comparatively rapid course, and, at times, irregular progression, periods of arrest alternating with exacerbations.

*Infantile Progressive Spinal Muscular Atrophy* (*Werdnig-Hoffmann Type*).—This rare disease develops in early childhood and is usually of an hereditary and familial character. It is marked by progressive atrophic paralysis, which begins in the muscles of the thigh and pelvic girdle, then involves the muscles of the trunk, and later on attacks the muscles of the legs and arms in a descending order. There may be some tendency to obesity, but pseudo-hypertrophy is absent. Fibrillary twitching is rarely seen. The mental condition is good, sensation is normal and the sphincters remain intact. Death occurs in from 1 to 5 years after the onset, usually from paralysis of the respiratory muscles or bronchopneumonia.

**Diagnosis.**—*Amyotrophic lateral sclerosis* is distinguished by the occurrence of spastic symptoms in the legs, exaggerated tendon reflexes, and the almost constant tendency to bulbar paralysis. *Primary muscular dystrophy* begins in childhood, is preëminently an hereditary and familial disease,

usually attacks first the proximal muscles and those of the trunk, is frequently productive of pseudohypertrophy in certain parts, especially the calves, and rarely, if ever, produces fibrillary tremors or reactions of degeneration. Hereditary spinal muscular atrophy of childhood without fibrillary tremors or reactions of degeneration may be difficult to distinguish from hereditary muscular dystrophy. However, the appearance of the symptoms in the first 2 or 3 years and a rapid course are in favor of spinal muscular atrophy. *Syringomyelia, multiple neuritis* and *cervical hypertrophic meningitis* may usually be distinguished from progressive spinal muscular atrophy by the presence of subjective and objective sensory disturbances. Atrophy of the thenar eminence or intrinsic muscles of the hands, the result of *professional neuritis*, if unaccompanied by paresthesia, may bear such a strong resemblance to spinal amyotrophy that the diagnosis between the two conditions must be left in doubt, at least for a time. It is highly probable that some of the cases of progressive muscular atrophy which have been reported as ending in recovery have really been examples of professional neuritis. *Progressive neural muscular atrophy* (*Charcot-Marie-Tooth* type) differs from *hereditary spinal muscular atrophy of childhood* (*Werdnig-Hoffmann type*) in beginning in the distal portion of the limbs, especially the legs, and in producing, as a rule, sensory disturbance. Transitional forms, however, are observed. *Arthritic muscular atrophy* is not likely to come into question as it is limited to muscles in the neighborhood of stiff, painful joints.

**Prognosis.**—The prognosis is unfavorable, although in the Duchenne-Aran type the course may extend over many years. Death usually results from some intercurrent disease.

**Treatment.**—Muscular fatigue has a deleterious influence and should be avoided. Massage and electricity are of little service. Strychnin has been recommended by Gowers, but it does not appear to influence the progress of the affection. If there are evidences of syphilis (positive Wassermann reaction, scars on the skin, lymphocytosis of the cerebrospinal fluid, etc.) antiluetic remedies should be given a thorough trial.

## CHRONIC PROGRESSIVE BULBAR PALSY

Chronic progressive bulbar palsy, or progressive glosso-labio-laryngeal paralysis, is a slowly advancing symmetrical degeneration of the motor nuclei of the cerebral nerves in the medulla oblongata and pons. In the majority of cases it is a part of amyotrophic lateral sclerosis (*q.v.*), the gangion cells in the anterior horns of the spinal cord and the pyramidal tracts being also implicated. In rare instances, however, the bulbopontine nuclei alone are involved.

The causes of the disease are unknown. In some cases syphilis is apparently a factor, and occasionally a family tendency is observed. More males are attacked than females. The age of onset is, as a rule, between 30 and 50.

**Symptoms.**—The onset is gradual and usually the first symptom to attract attention is difficulty in pronunciaton, especially of the linguals (D., R., L., Sh., etc.) and labials (P., M., F., W., U., etc.). Ere long the pharyngeal and palatal muscles become affected and then the voice acquires a nasal quality, dysphagia is experienced, saliva accumulates in the mouth, and food tends to enter the posterior nares. After the orbicularis oris has become involved it is impossible for the patient to whistle or blow, to close the mouth completely, or to prevent the saliva from druling. Eventually,

mastication becomes seriously impaired, owing to weakness of the pterygoid muscles and the inability of the tongue to keep the food between the teeth; paroxysms of coughing and suffocation occur frequently because of the entrance of food or saliva into the larynx; and the voice become monotonous and feeble in consequence of paresis of the laryngeal muscles. Spontaneous attacks of dyspnea and of acceleration or irregularity of the cardiac contractions may also occur as a result of involvement of the nuclei of the pneumogastric nerves. In the later stages of the disease the lower part of the face is rigid and expressionless, the lips are thin, parted, and festooned with saliva, and the tongue, wasted and wrinkled, lies motionless on the floor of the mouth. The muscles of the forehead and eyes usually functionate normally, but occasionally these are also affected. The reflex and electrical excitability of the paralyzed muscles is, as a rule, diminished and fibrillary twitchings are commonly present. The mind is clear to the last, but a peculiar emotional state with obsessional laughing and crying is not infrequently noted. Progressive bulbar palsy always proves fatal, death occurring, as a rule, in from one to three years in consequence of deglutition pneumonia, suffocation or syncope.

**Diagnosis.**—This usually offers no great difficulties. *Acute bulbar paralysis*, due to infection (acute poliomyelitis) or to thrombotic occlusion of the basilar or of the vertebral arteries, makes itself known by a sudden onset and frequently by alternating hemiplegia and alternating hemianalgesia. The condition known as *pseudo-bulbar paralysis*, which results from bilateral (usually vascular) lesions in the brain involving both cortico-bulbar pathways, resembles progressive bulbar paralysis, but it may usually be distinguished by the history of a sudden onset with unconsciousness, or of several successive apoplectic attacks, each of which has changed somewhat the distribution of the paralysis, by the coexistence of unilateral or bilateral hemiplegia and of psychic disturbances, and by the absence of atrophy, fibrillary tremors, and electrical changes in the paralyzed muscles. In *asthenic bulbar paralysis* (*myasthenia gravis*) there is no real atrophy of the muscles or dribbling of saliva, the symptoms vary remarkably in severity from time to time and are always aggravated by exertion, the extremities are frequently affected, and ocular palsies, especially ptosis, are present in the majority of cases. Furthermore, muscular contractility quickly disappears with a tetanizing faradic current and quickly returns when the muscle is allowed to rest (myasthenic reaction).

**Treatment.**—As no treatment is known to check the progress of the disease, it is best to aim at promoting the patient's general health by rest, careful feeding, hydrotherapy, massage, and the administration, if necessary, of tonic remedies. When food can no longer be swallowed, recourse should be had to the feeding tube.

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# DIFFUSE AND FOCAL DISEASES OF THE SPINAL CORD

## DISSEMINATED CEREBROSPINAL SCLEROSIS

**Definition.**—Disseminated, multiple, or insular cerebrospinal sclerosis is a chronic disease characterized anatomically by islets of sclerotic tissue scattered irregularly throughout the central nervous system.

**Etiology.**—The affection appears to be comparatively rare in this country, although doubtess it often fails of recogniton. In the large majority of cases the symptoms develop in early adult life, between the fifteenth and thirty-fiith years. Males are somewhat more frequently affected than females. An hereditary or familial tendency has occasionally been noted. The history of an acute infection shortly before the onset is often obtainable. In a number of instances poisoning by one of the metals has been an antecedent condition. In other cases, exposure to cold, trauma, or fatigue seems to have had an etiologic or augmentative influence. Syphilis apparently plays no part in the causation of the disease.

**Morbid Anatomy and Pathogenesis.**—Anatomically, the characteristic feature is the presence of more or less numerous sclerotic plaques throughout the brain and spinal cord. These plaques, which are of a grayish or grayish-red color and usually sharply defined, range from a millimeter to several centimeters in diameter. According to age, they may be softer or firmer than the healthy tissue. The white matter is usually more extensively involved than the gray, and in the brain the preferred sites are the centrum ovale, corpus callosum, pons and medulla. The cranial nerves are affected in many cases.

*Histologically*, there is an increase of glia tissue with a dense or loose interlacement of the fibers, according as the patch is firm or soft. The nerve elements within the diseased patches suffer less than in other sclerotic processes, as is shown by the axis cylinders remaining intact long after the myelin sheaths have disappeared. This preservation of the axis-cylinders doubtless accounts for the rarity with which secondary degeneration is observed. Marked alterations in the ganglion cells are also unusual. The pathogenesis of the disease is obscure. While it is generally admitted that the lesions are of toxic origin, much difference of opinion exists as to the nature of the poison and the manner of its action. It is probable that the nerve-fibers are first affected, although many eminent authorities oppose this view, some believing that the process begins in the vessels, others regarding the glia increase as the primary change (multiple gliomata).

**Symptoms.**—The symptoms vary, of course, with the site of the lesions and the extent of the damage. In well-developed cases, however, there are commonly four conspicuous manifestations, namely, paresis, tremor, nystagmus and disturbance of articulation.

The *paresis* usually begins in the lower extremities and is almost always of the spastic type. Frequently it is more marked on one side than the other or is confined for a time to one member. In some cases the arms are chiefly affected, and occasionally the disability takes the form of a progressively developing hemiparesis, beginning in an arm or a leg and later involving the other limb of the same side. The tendon reflexes are, with rare exceptions, exaggerated and Babinski's sign is nearly always present. The abdominal reflex, however, is usually lost.

Atrophy of the muscles is scarcely ever observed. The gait is usually of the spastic-paretic form or partly of this form and partly swaying or zigzagging as in cerebellar disease. Disturbances of the bladder are superadded to the paresis at some period or other in about four-fifths of the cases. A *tremor*, which appears only when voluntary movements are undertaken, and therefore is known as an *intention tremor*, is a very common symptom. It is most distinct, as a rule, in the upper extremities, particularly in the hands, and is well shown when the patient attempts to write or to raise a glass full of water to his lips. Closely related to the tremor is *nystagmus*, or oscillation of the eyeballs, which is observed in more than one-half of all cases when the patient turns his eye laterally or upward or gazes steadily at a near object.

Somewhat less frequent than tremor and nystagmus, but probably allied to these phenomena in the manner of its production, is a characteristic defect of articulation, known as the *scanning* or *staccato speech*. The patient talks in a slow, hesitating, monotonous way, pausing between the words or syllables, as if scanning a line of poetry.

In addition to these classical symptoms there are many others of more or less significance. Included among the latter are certain ocular phenomena other than nystagmus, disturbances of sensation, psychic alterations, apoplectiform attacks, and vertigo.

*Impairment of vision*, not rarely confined to one eye and frequently remittent, may be the earliest manifestation of the disease. It sometimes occurs without objective findings in the eye. An especially common disturbance is central scotoma, the result of retrobulbar neuritis; indeed, the occurrence of the latter in a young person without obvious cause should always excite suspicion of multiple sclerosis. Peripheral contraction of the visual fields is sometimes observed, but it is less frequent than central scotoma. *Optic atrophy* with pallor of the disc develops in more than one-half of all cases. It is rarely uniform, and for a long time is often confined to the temporal side. Transient paresis of the extrinsic ocular muscles is also relatively common. Disturbances of the pupillary reflexes are exceptional.

*Sensory disturbances* are not often conspicuous and usually consist of transient paresthesias. In some cases, however, objective sensory defects are observed in the distal portions of the limbs and occasionally there is ataxia of the tabetic type. *Psychic alterations* are not uncommon and sometimes precede the other symptoms by months or years. The usual disturbance is a variable degree of dementia with euphoria or, less frequently, depression, but occasionally there is an expansive delirium suggestive of general paresis, or a mental state simulating manic-depressive insanity. Obsessional laughing or crying is somewhat frequently observed. *Apoplectiform attacks*, sometimes accompanied by epileptiform seizures and not rarely followed by transient paralysis, occur in a fairly large proportion of all cases. *Vertigo* is relatively frequent and may appear early in the disease. The *cerebrospinal fluid* reacts negatively to the Wassermann test and shows an absence of pleocytosis and a normal protein content.

In some cases the spinal symptoms predominate, in others the cerebral phenomena are most conspicuous, and rarely bulbar manifestations—indistinct articulation, difficult deglutition, laryngeal palsy, increased salivation—are the obtrusive features.

**Onset and Course.**—The onset, although usually gradual, is sometimes acute or even abrupt. Paresis in one or more of the limbs, paresthesia, vertigo, tremor, ataxia, and impairment of vision are the commonest initial symptoms. In a large proportion of cases the disease is not steadily progressive, but marked by more or less frequent remissions and relapses. Indeed, a pronounced ebb and flow of symptoms, especially in the early stages, is rather characteristic. Instances in which paresis or amblyopia have disappeared and after the lapse of months or even years have reappeared are by no means rare. The duration of life is, as a rule, between 5 and 15 years. Ocasionally, however, death occurs within a few months of the onset (Ribbert, Marburg, Buzzard, Bramwell).

**Diagnosis.**—Disseminated sclerosis in the early stages may readily be confused with *hysteria*. The latter, like the former, usually occurs in young adults and is not rarely ushered in with transitory paresis, paresthesia, or amblyopia. Moreover, the two conditions occasionally coexist in the same patient. Usually, however, a careful study of the symptom-complex will reveal some evidence of organic disease, if such exists. Ankle clonus,

Babinski's sign, nystagmus, changes in the optic discs, and incontinence of urine are strongly opposed to a functional disorder.

Great difficulty may be experienced in distinguishng between *cerebellar tumor* and disseminated sclerosis, and in certain cases the decision must remain in doubt, at least for a time. In favor of the former are severe headache, vomiting, and intraocular optic neuritis, and in favor of the latter are ankle clonus, Babinski's sign, disordered micturition, and, retrobulbar neuritis with central scotoma and pallor of the disc, especially on the temporal side.

The differential diagnosis between multiple sclerosis and *cerebrospinal syphilis* can usually be made without much difficulty. Rigidity of the pupil, paroxysmal somnolence, severe nocturnal headache and lymphocytosis of the cerebrospinal fluid with a positive Wassermann reaction point strongly to syphilis, while intention tremor, nystagmus, syllabic speech, and signs of retrobulbar neuritis are highly suggestive of multiple sclerosis. The ordinary form of disseminated sclerosis in which there are cerebral manifestations, sensory disturbances and sphincteric disorders can scarcely be mistaken for *primary lateral sclerosis*, but in cases in which spastic paresis is the chief symptom differentiation may be impossible. Paraplegic cases of multiple sclerosis may also be readily confused with *spinal tumor*. In a number of instances laminectomy has been done owing to an error in diagnosis. *Paralysis agitans*, although it is productive of a tremor and of increased tonicity, can scarcely be mistaken for disseminated sclerosis, as it is a disease of old persons, and its tremor is of small amplitude and is not intentional or volitional. The differentiation of multiple sclerosis from *family cerebellar ataxia* is considered on p. 987, and from *progressive lenticular degeneration* on p. 974.

The very rare conditions known as *diffuse sclerosis*[1] and *pseudosclerosis*[2] which occur especially in early life, cannot be distinguished with certainty either from one another or from disseminated sclerosis. Diffuse sclerosis, which is characterized anatomically by abnormal hardening of the brain and cord, the consequence of widespread neurogliar proliferation, is probably a more advanced form of so-called pseudo-sclerosis, although in some cases of the latter the findings appear to have been absolutely negative. The most distinctive features of these conditions seem to be the development of the symptoms, as a rule, in childhood or youth, the early and pronounced dementia, the relative frequency of epileptiform attacks, and the relative rarity of nystagmus, optic atrophy and sphincteric disturbances.

**Treatment.**—This is wholly palliative. Rest, luke-warm baths, and gentle massage sometimes favorably influence the rigidity. Forced feeding may be necessary. Overexertion, mental excitement, sexual excesses, and the use of alcohol and tobacco are to be avoided. If there is anemia, iron and arsenic are indicated. Improvement has been reported from the use of roentgen rays (Marinesco) and also from intramuscular injections of fibrolysin (Crafts).

## MYELITIS

**Definition.**—By the term myelitis is usually meant a more or less rapid, complete, and extensive destruction of the substance of the spinal cord

[1] Strümpell, Arch. f. Psych., 1878, ix.

[2] Westphal, Arch. f. Psych., 1883, xiv; Frankl-Hochwart, Arb. aus dem Neurol. Inst. an der Wien. Universität, 1910, Heft 10; Potts and Spiller, Jour. Amer. Med. Assoc., Nov. 11, 1905.

consequent on ischemia from vascular occlusion, on inflammation, or on the direct action of certain toxic agencies, but not on actual laceration, large hemorrhages or the breaking down of neoplasms. In many cases myelitis is due to thrombosis the result of disease of the bloodvessels, and is therefore analogous to cerebral softening. In some instances, however, inflammation is clearly the primary factor and occasionally a necrosis of the nervous elements of toxic origin appears to be the initial lesion.

**Etiology.**—*Syphilis* is responsible for many of the cases. The time elapsing between the appearance of the primary sore and the development of the first spinal symptoms varies from six months to ten years or more. The *acute infections*, such as typhoid fever, smallpox, scarlatina, cerebrospinal fever, septico-pyemia, gonorrhea, and rabies are etiological factors of some importance, but their influence is small compared with that of syphilis. A *tuberculous form* occasionally occurs in connection with caries of the vertebræ. *Active immunization from rabies* is occasionally followed by a condition strongly indicative of myelitis. *Certain poisons other than bacterial toxins* are capable of producing the disease. Thus, a degenerative type of myelitis has been observed in alcoholism, in ergotism, and in poisoning by arsphenamin, illuminating gas, carbon disulphide, etc. The myelitis very rarely occurring during pregnancy is probably the result of some obscure autointoxication. Not infrequently the disease may be traced directly or indirectly to *trauma*. Even concussion of the spine without injury to the vertebræ may be followed by hemorrhages and necrosis in the gray matter of the cord. As the softening in the cord consequent on compression in such conditions as Pott's disease, tumors of the vertebræ or meninges, syphilitic spondylitis, arthritis deformans of the spinal column (spondylose rhizomélique) and aneurysm of the aorta is due in large part to mechanic obstruction of the bloodvessels and may be accompanied by reactive processes of an inflammatory nature, it is not inappropriately termed *compression-myelitis*. Occasionally acute or subacute myelitis (spinal thrombosis with softening) occurs in old persons as a result of *sclerosis of the spinal vessels*. A number of cases of spinal abscess secondary to bronchiectasis are on record and instances of intramedullary suppuration in connection with cystitis are cited by Schlesinger, Sternberg and others.

**Bacteriology.**—In some cases of infective myelitis streptococci, staphylococci, pneumococci, typhoid bacilli or tubercle bacilli are found in the tissues of the cord, but in degenerative forms of the disease bacteria are rarely present.

**Morbid Anatomy.**—Myelitis is said to be *diffuse* when a considerable length of the cord is affected, *transverse* when the entire thickness of the cord is involved for a comparatively short distance, and *disseminated* when a number of diseased foci are distributed throughout the cord. Inflammation limited to the gray matter is known as *poliomyelitis*, but as this type has a special etiology and presents a distinct clinical picture it requires separate consideration (see p. 264).

An examination of the cord does not always reveal gross changes. In the more severe forms of myelitis, however, it is usual to find evidences of meningitis over the affected areas and changes in the consistency and color of the diseased tissue. In early cases the latter is commonly more or less softened, edematous, and of a pinkish, reddish or brownish-red hue, according to the quantity and state of the extravasated blood. In the most intense forms the substance of the cord may be so soft that it flows out as a creamy puriform fluid when the membranes are cut. On the other hand, in long-standing cases the diseased portions of the cord are usually shrunken, firmer than the normal tissue, and of a grayish color.

*Microscopic examination* of the affected areas always reveals more or less destruction of the parenchyma. In recent cases the myelin sheaths are swollen and nodose or have partially disappeared. The axis-cylinders are swollen, varicose, and often broken. The ganglion-cells, if not completely disintegrated, are rounded, homogeneous, translucent looking, and without processes. Many of the neuroglia-cells are enlarged, vacuolated and multinuclear. At times they are increased in number. Intermingled with the detritus of the nervous elements are free myelin drops, fat globules, compound granule-cells and leucocytes. Hemorrhagic extravasations are often observed. Inflammatory changes—engorgement of the bloodvessels and perivascular round-cell infiltration—may be a prominent feature, but more frequently these are inconspicuous, and the chief vascular lesion is the one that has caused the other alterations, namely, endarteritis with obstructive thrombosis.

In long-standing cases the nervous elements which have been destroyed are replaced by overgrown neuroglia (sclerosis) and the sensory tracts extending upward from the myelitic focus and the motor tracts extending downward from it are the seat of secondary degeneration.

In syphilitic acute myelitis the dorsal region of the cord is usually affected, and the changes are, as a rule, those of softening secondary to disease of the bloodvessels. In some instances, however, there are evidences of infiltration of a granulomatous or gummatous nature. In the myelitis accompanying Pott's disease the primary change in the cord is edema from stasis of blood and lymph (Schmaus), and the factor immediately responsible for this circulatory disturbance is pressure from tuberculous granulation tissue in the dura or an intraspinal abscess, rather than actual displacement of the vertebræ.

**Symptoms.**—The clinical picture of myelitis depends not only upon the height and transverse extent of the lesions, but also upon whether the chief motor and sensory tracts are completely or incompletely interrupted, and whether the meningeal coverings and nerve-roots are involved or not. Generally speaking, there are (*a*) atrophic paralysis of the muscles innervated by the segments of the cord in which the disease is situated; (*b*) flaccid paralysis with abolition of all reflexes in the parts supplied from the cord below the lesion, if the latter is profound,[1] or spastic paralysis with exaggerated tendon-reflexes and diminished skin reflexes, if the lesion is slight; (*c*) more or less loss of sensation over all parts innervated from the cord below the level of the disease; (*d*) vesical and rectal disturbances; and (*e*) trophic changes in the skin, especially bedsores, if all impulses are completely interrupted. If the spinal membranes or posterior roots are affected, as in meningo-myelitis, stabbing pain referred to a segmental skin area, hyperesthesia, and paresthesia are usually present, at least at the onset of the attack. Chills and fever are seldom observed except in the comparatively uncommon infectious or inflammatory cases. Occasionally, owing to the participation of the brain in the process, optic neuritis precedes, accompanies or follows the myelitic phenomena.

*Transverse Dorsal Myelitis.*—This is manifested chiefly by paraplegia (spastic with partial, and flaccid with complete lesions); loss of sensation in the lower half of the body, varying in degree from slight tactile hypesthesia to complete anesthesia for all forms of sensation; partial or complete incontinence of urine and feces, and a tendency to acute bedsore (decubitus). Cyanosis, edema, and anomalies of secretion in the paralyzed parts may also appear. Atrophic paralysis of the trunk muscles is not often conspicuous,

[1] The flaccidity of the muscles is ascribed to the complete cutting off of the tone-maintaining impulses emanating from the cerebral cortex.

because these muscles are supplied by a number of segments. If the patient survives, a paraplegia that is at first flaccid usually becomes spastic in the course of a few days or weeks.

*Transverse Cervical Myelitis.*—Acute disease of the upper cervical segments usually proves rapidly fatal owing to paralysis of the respiratory muscles. Disease of the lower cervical segments is characterized by flaccid paralysis of the flexors of the wrist and small muscles of the hand; paralysis of all the muscles below the arms (except the diaphragm), of a spastic type if the lesion is partially destructive, and flaccid if it is completely destructive; more or less complete loss of sensation in the arms, trunk, and legs; interference with respiration; paralysis of the sphincters; tendency to bedsores; and in some instances by sympathetic miosis and ptosis (Klumpke's paralysis).

*Transverse Lumbar Myelitis.*—Acute disease of the lumbar cord usually gives rise to flaccid atrophic paraplegia, paranæsthesia, incontinence of urine and feces, and bedsores. If only the upper lumbar segments are affected, however, the paralysis of the toes may be spastic and ankle clonus and Babinski's reflex may be elicited.

*Acute Ascending Myelitis*—In this form of myelitis the paralysis of motion and sensation begins in the lower limbs and more or less rapidly ascends until the muscles of respiration are affected, when death usually supervenes.

*Compression Myelitis.*—In this condition three groups of symptoms are commonly recognizable, one referable to the vertebræ, another to the nerve-roots, and a third to the cord itself. Generally the symptom-groups appear in the order mentioned, but exceptions to this rule are sometimes observed. The vertebral symptoms consist of localized pain, dull deep-seated, and increased by jarring or flexing the spine; tenderness over one or two spinous processes, rigidity of the affected part of the spinal column, and, in most cases, deformity. Roentgenographic studies may be a valuable aid in diagnosis. The root symptoms are variable. The most constant is severe stabbing pain referred to the peripheral distribution of the afferent nerves, the roots of which are involved in the compression. Hyperesthesia and later hypesthesia may also be observed in the same regions.

Muscular spasm or paralysis of radicular origin is rarely a conspicuous feature. Occasionally, herpes zoster occurs from involvement of a spinal root ganglion. The signs of compression of the cord vary with the level of the disease and the degree of interference with the conductivity of the afferent and efferent tracts. Speaking generally, spastic paresis with exaggerated reflexes and paresthesia or hypesthesia develops in parts supplied by the cord below the level of the lesion. After a time, if the conductivity of the cord is completely destroyed, the paraplegia may become flaccid and the reflexes may disappear. As in other forms of myelitis, incontinence of urine and feces, sexual impotence with a tendency to priapism, and trophic changes in the skin are noted when the lesions are severe.

**Course.**—The onset of myelitis varies more or less with the type of the disease. In some cases of softening of the cord from vascular occlusion it is abrupt without premonition (myelitis apoplectica). In syphilitic softening, however, symptoms of spinal irritation are usually present for several days or weeks before paralysis sets in. Myelitis the result of the specific fevers develops acutely, and is generally ushered in with chills and pyrexia. On the other hand in the compression form the onset of paralysis is, as a rule, gradual. Once established myelitis may run its course to a fatal ending in a few days, or it may continue for several weeks when death may occur from some complication or partial recovery ensue, a variable degree of spastic

paresis remaining as a permanent sequel. Except in very mild attacks, a complete restoration of function is rarely observed. The course of the disease is not always uniformly progressive, marked fluctuations in the intensity of the symptoms sometimes occurring, especially in syphilitic cases. When improvement sets in the sensory disturbances usually disappear before the motor. In fatal cases the cause of death may be paralysis of the respiratory musculature, hypostatic pneumonia, a septic condition following a large bedsore, or cystitis with consequent pyelonephritis. Complete flaccid paralysis with incontinence of urine and feces is always of the gravest import, even when it is known to be of syphilitic origin.

**Diagnosis.**—The differential diagnosis of *multiple neuritis* and of *Landry's disease*, which resemble myelitis in several respects, is considered on pages 907 and 1004 respectively.

*In acute poliomyelitis* the paralysis usually involves only certain groups of muscles, there is no loss of sensation, and the sphincters are rarely disturbed. In *spinal meningitis* pain, rigidity of the spine, and Kernig's sign are conspicuous features, while signs of paralysis, at least at first, are ill defined, and, further, the changes in the cerebrospinal fluid are usually decisive. Compression myelitis is occasionally simulated by disseminated sclerosis and by amyotrophic lateral sclerosis. In *disseminated sclerosis*, however, the onset is usually more gradual than that of myelitis, ocular symptoms (nystagmus, amblyopia, optic atrophy, paresis of ocular muscles) and disturbances of articulation often appear early, pain in the limbs is rarely pronounced, and objective sensory changes are, as a rule, slight. *Amyotrophic lateral sclerosis* is distinguished from compression of the cervical cord by the complete absence of sensory symptoms.

**Treatment.**—If possible the patient should be placed on a water-bed or air-bed. If there is evidence of syphilis antiluetic treatment should be instituted. Every precaution must be taken to prevent the development of bedsores. Frequent change of the patient's position, absolute cleanliness of the parts subjected to pressure, and bathing with alcohol and water will do much toward averting this serious complication. Retention of urine must be met by systematic catheterization under strict aseptic precautions. When there is incontinence a carefully adjusted urinal should be employed. Any tendency to cystitis will demand daily irrigation of the bladder with mild antiseptic solutions. Spastic paresis is best treated by warm baths and passive movements. If the patient improves he should be encouraged to carry out himself simple gymnastic exercises and to attempt stepping and other movements, since by so doing he is likely to cultivate a certain amount of compensatory function in tracts of the cord that have not been destroyed.

The treatment of paraplegia the result of spinal caries consists in absolute rest in the recumbent position, fixation and progressive straightening of the spine, and, if necessary, the performance of Albee's bone-grafting operation or laminectomy.

## CHRONIC MYELITIS

Aside from the chronic process remaining in the cord after acute or subacute myelitis and that which develops in connection with chronic meningitis of tuberculous or syphilitic orign (chronic meningo-myelits) there is no condition that deserves the name of chronic myelitis, unless it be the *syphilitic spinal paralysis of Erb.*[1] This affection is characterized by slowly developing spastic paraparesis, exaggerated tendon reflexes, retention or incontinence

[1] Neurolog. Centralbl., 1892, No. 6.

of urine, paresthesia, and some impairment of sensation, especially to pain and temperature. Even in cases presenting these symptoms the pathologic changes probably depend upon endarteritis and interference with the vascular supply of the cord, if not upon actual thrombosis, and are therefore not far removed from those of syphilitic transverse myelitis. Among conditions which have often been regarded as chronic myelitis in the past may be mentioned amyotrophic lateral sclerosis, disseminated sclerosis, subacute combined degeneration of the cord, syringomyelia, compression paraplegia due to vertebral disease or tumors, and arteriosclerosis of the spinal cord.

## LANDRY'S DISEASE

### (Acute Ascending Paralysis)

The chief feature of the comparatively rare symptom-complex known as Landry's disease, as described by the observer[1] whose name it bears, is an acute paralysis, flaccid in character, beginning in the legs, rapidly ascending to the trunk and arms, and finally causing death, usually within a week, by involvement of the muscles innervated from the medulla. This paralysis usually spares the sphincters and is unaccompanied by pronounced disturbances of sensation, trophic changes in the affected muscles, mental symptoms or any distinct febrile reaction.

Since the appearance of Landry's original publication many cases have been reported by competent observers as examples acute of ascending paralysis in which the clinical picture has diverged to a greater or less extent from that drawn by Landry himself. Thus, in some instances there have been not only considerable numbness and tingling, but actual pain; in others, a certain degree of muscular atrophy with electric changes has been noted; in others still the sphincters have been involved; and occasionally the paralysis has been descending or centripetal rather than ascending, the muscles of the arms or those supplied by the bulbar nerves having been involved before those of the legs.

The disease, although doubtless always of infectious or toxic origin, is probably the result of no one particular organism or poison. In many cases it has developed without recognizable etiologic relations, but not rarely it has followed closely upon one of the specific fevers or has occurred in association with septicemia, gonorrhea, cystitis or syphilis. Several varieties of bacteria have been noted by various observers as occurring in the tissues after death and, further, enlargement of the spleen and tumefaction of the lymph-nodes have been common findings at necropsies.

The **morbid anatomy** of the disease is variable. The earlier examinations gave, as a rule, negative results and Landry himself considered "an absence of all appreciable nervous lesions" important evidence in identifying the syndrome. More recent examinations by Nissl's method, however, have usually revealed definite changes in the nervous system, particularly degeneration of the peripheral nerves, of the ganglion cells in the anterior horns of the spinal cord, or of both nerves and cells. Acute inflammatory lesions in the anterior horns have also been frequently noted, especially in children. It is probable, therefore, that the inciting agent of Landry's paralysis, whatever its nature, acts chiefly upon the lower motor neurons, the peripheral processes in some instances, the cell bodies in others, bearing the brunt of the attack, and that the disease is closely related in some cases to acute anterior

[1] Landry; Sur la paralysie ascendante aiguë, Gaz. hebdom, 1859, vol. vi.

poliomyelitis, in others to acute infective multiple neuritis, and in others still to acute ascending myelitis. If this conception of the morbid process be correct one can readily understand why at times it is absolutely impossible to decide in which of the three categories a case of ascending paralysis belongs. Ordinarily, in *acute poliomyelitis*, however, the process ceases before the anterior horns throughout the entire length of the cord are affected, the medulla is not involved, the paralysis is limited to certain groups of muscles and is in the extremities only, and atrophy and electric changes occur in the affected muscles. The absence of trophic changes in Landy's paralysis is doubtless commonly due to the short duration of the disease.

In *multiple neuritis* of the ordinary type the sensory neurons are affected as well as the motor, sensory disturbances are pronounced, the nerve-trunks are tender on pressure, the nerves innervated from the medulla usually escape, the course is less rapid, and the outcome is generally favorable.

*Acute ascending myelitis* may usually be recognized by the occurrence of complete and permanent paralysis of the sphincters, the presence of objective sensory disturbances, especially marked anesthesia, and by the tendency to bedsores or other trophic changes in the skin.

In *family periodic paralysis* the picture presented may for a time be not unlike that of Landry's disease but the onset is even more sudden, than in the latter, the electric excitability of the affected muscles is markedly diminished or lost, and the paralysis usually disappears as rapidly as it came in from a few hours to two or three days.

Landry's disease is usually fatal, but recovery, partial or complete, may occur. A great majority of the cases terminate in from a few days to two or three weeks. Treatment should be supportive and mildly eliminative. Counterirritation to the spine is to be avoided.

## CAISSON DISEASE

**Definition.**—The term caisson disease or diver's palsy is applied to the various disturbances, chiefly nervous, which frequently occur in persons who have been subjected to a high atmospheric pressure when their return to the ordinary atmospheric pressure has been effected too quickly.

**Etiology.**—Workers in caissons, submarine tunnels, and diving bells are the principal sufferers. The symptoms never develop while the individual is under the excess of pressure, but appear in from a few minutes to several hours after his arrival at the surface. As Paul Bert[1] first pointed out in his classic monograph on the subject, the duration and the length of time occupied by decompression play parts in the etiology of the disease scarcely less important than the degree of pressure. Other factors are the age and physical condition of the worker and the temperature of the air in the working chamber. Young, healthy, lean men can usually work with comparative safety for periods of three or four hours each under a pressure of 2–2½ atmospheres (30–38 pounds), provided the chamber is cool and well ventilated, and sufficient time (10 to 20 minutes) is allowed for decompression. Virtually no cases occur at a pressure below 2 atmospheres.

**Pathogenesis and Morbid Anatomy.**—It is generally conceded that the symptoms of caisson disease are due to the rapid liberation of nitrogen, large quantities of which are absorbed from the atmospheric air by the blood and tissues during the period of compression. When decompression

[1] La Pression Barométrique, Paris, 1878.

is effected slowly the dissolved gas gradually escapes in the more rarefied air of the lungs, but when decompression is hurried, the gas is given off in bubbles, which through fusion may become sufficiently large to plug small vessels and cause foci of ischemic necrosis or even to produce pulmonary embolism.

In the few cases that have come to necropsy the important findings have been free collections of gas in the blood and solid tissues, congestion of the organs, and in the central nervous system, particularly the spinal cord, foci of softening, minute hemorrhages, or actual fissures. The spinal cord usually bears the brunt of the injury, probably because it is especially rich in fatty matter which has a strong solvent affinity for nitrogen and also because it has a relatively poor blood supply.

**Symptoms.**—Various groups of symptoms are observed. The most common group—the "*bends*"—consists of severe pain in the limbs, especially in the legs about the knees, abdominal cramps, itching or numbness of the skin, and retention of urine. Occasionally, dyspnea and cough are also present—the "*chokes*." In other cases there is a true paralysis, usually paraplegia, with retention or incontinence of urine, and impairment of sensation. Vertigo, staggering, dimness of vision, tinnitus aurium, neuralgic pain and nausea constitute another group—the "*staggers*." The worst forms are marked by general collapse, vomiting, cyanosis, mottling of the skin, and unconsciousness. Bleeding from the nose or into the skin is sometimes observed.

Among 352 workers employed on the St. Louis bridge (4⅓ atmospheres) there were 119 cases of caisson disease, 56 being cases of paralysis, and 14 deaths. During the construction of the East River tunnels at New York (3 atmospheres), with better regulations, there were 3,692 cases, but only 20 deaths, 88 per cent. of the cases being of the type known as "bends." Unless cerebral or circulatory symptoms are conspicuous there is little danger to life. Pain and paralysis usually disappear completely in a few days, but the latter may persist for months, with all the features of myelitis, and occasionally it is permanent.

**Treatment.**—The prophylaxis has already been indicated in citing the etiologic factors. The higher the pressure the shorter should be the shifts and the longer the time allowed for decompression. Boycott, Damant and Haldane[1] have shown, however, that it is safe to decompress from any stage whatever by successive reduction of one-half at a time. This method is known as "stage" decompression in contradistinction to the older practice of a slow uniform rate of reduction. Stage decompression is materially aided by active physical excercise and oxygen inhalations, which facilitate the expulsion of nitrogen. With regard to treatment, nothing is so efficacious as recompression followed by gradual decompression, but it is important that these measures should be carried out promptly to prevent permanent damage to the tissues. Recompression cured 90 per cent. of the cases in the East River tunnel and partly relieved all but 0.5 per cent. Other treatment is symptomatic. Collapse will call for appropriate stimulation, retention of urine for catheterization, and neuralgic pains for warm applications, massage and anodynes. The after-treatment of paralytic cases should be that of myelitis.

[1] Jour. of Hyg., 1908, viii, 342.

## SYRINGOMYELIA

**Definition.**—Syringomyelia[1] is a chronic slowly progressive disease of the spinal cord characterized anatomically by the presence in the gray matter of one or more tube-like cavities surrounded by an overgrowth of glia tissue and manifested clinically in its ordinary form by muscular atrophy, paresis, dissociated anesthesia, and various trophic disturbances in the skin, joints and bones.

**Etiology and Pathogenesis.**—The disease, which is comparatively rare, is more frequent in males than in females, and usually shows itself between the ages of 10 and 40 years. In some cases trauma or a preceding infection seems to have stood in a causal relationship. In a few instances several members of a family have been affected. The pathogenesis is somewhat obscure and probably not uniform. It is generally accepted, however, that in the majority of cases the cavity formation originates in an anomaly of development, being produced by the breaking down of a congenital overgrowth of glia tissue (primary gliosis) or by the proliferation and subsequent liquefaction of nests of ependyma-cells which have persisted behind the central canal or, perhaps, along the line of closure. In exceptional cases the cavities seem to owe their existence to hemorrhage, the result of traumatism, to ischemic softening, the consequence of vascular occlusion, or to the breaking down of a true tumor (glioma).

**Morbid Anatomy.**—As a rule, there is but one cavity and this in most cases is in the cervicodorsal region. Any portion of the cord, however, may be affected, and occasionally a continuous passage is found extending from the medulla oblongata (*syringobulbia*), or even the pons, as far as the conus terminalis. The destructive process usually begins in the posterior commissure and thence invades the anterior and posterior horns, and at times the posterior columns. The lateral columns are not often excavated. Fusion with the normal central canal is sometimes seen. The cavity is usually filled with a watery or viscid liquid, which may be clear, turbid or sanious. Microscopic examination shows an irregular band of glia tissue of variable width about the cavity, sclerotic thickening of the bloodvessels, and frequently a loss of cells in the gray matter, with secondary degeneration in the posterior columns, pyramidal tracts, and nerve fibers, especially those of the anterior roots.

**Symptoms.**—The onset is insidious and usually marked by progressive muscular atrophy and disturbances of sensation. These symptoms are first noticed, as a rule, in the upper extremities and for a time may be limited to one member. In well developed cases the claw-like hand (main en griffe) and curvature of the spine are common deformities. The affected muscles are the seat of fibrillary twitchings and present changes in electric excitability, as in other forms of myelopathic atrophy. Subjective sensations, in the form of heat, cold, numbness or neuralgic pain, are of frequent occurrence, but by far the most constant and characteristic sensory disturbance is impairment or loss of the sense of temperature and pain with preservation of that of touch (dissociative anesthesia[2]). In a number of cases the first

[1] The word syringomyelia is from the Greek συριγξ, tube and μυελός, marrow.

[2] This phenomenon is explained on the supposition that thermal and painful impressions pass through the posterior gray commissure on their way to Gowers' tracts, while tactile impressions pass up through the posterior columns. It is not pathognomonic of syringomyelia, as it occurs also in some cases of tabes, tumor of the cord, leprosy, neuritis and hysteria, but with the other signs it is very suggestive. Pain sense may be tested by pricking the part with a pin and thermal sense by applying two small test-tubes of the same capacity, one containing hot water, the other cold.

indication of anything wrong was insensibility to burns or wounds. The thermo-anesthesia and analgesia are radicular in type and usually sharply limited by straight lines, appearing on the trunk as a series of transverse zones and on the limbs in glove-like or stocking-like areas.

Besides the muscles other tissues suffer in nutrition; thus, it is not unusual to find arthropathies (25 per cent. of cases), brittleness and deformity of the nails, abnormal fragility of the bones, glossy skin, chronic abscesses, and bullous eruptions. In the type known as Morvan's disease the formation of painless whitlows, leading in some instances to loss of substance and deformity of the fingers, is a prominent feature. Vasomotor and secretory disturbances consisting of cyanosis, erythematous and urticarial rashes, edema of the hands and hyperidrosis are of frequent occurrence. Ocular symptoms are also present is many cases. The most common are inequality of the pupils and nystagmus. Optic neuritis has been observed a few times, probably as a result of hydrocephalus, which is not a very rare complication. When the lateral columns are involved there is spastic paresis, usually in the legs; when the posterior columns are encroached upon ataxia is observed; and when the disease affects the medulla (syringobulbia) paralyses of the bulbar nerves, manifested by thermo-anesthesia and analgesia in the trigeminal area, hoarseness, difficulty in mastication and deglutition, hemiatrophy of the tongue, etc., are conspicuous symptoms.

**Diagnosis.**—This must be made by considering the whole group of symptoms present in the individual case. *Progressive spinal muscular atrophy* and *amyotrophic lateral sclerosis* may usually be distinguished by the absence of sensory symptoms, *chronic cervical pachymeningitis* by a period of severe pain in the neck and arms, and *hematomyelia* by the sudden or acute onset. *Tumor of the spinal cord* may closely resemble a localized syringomyelic cavity, but in the former severe pains are usually a conspicuous feature, the course is comparatively rapid, paralyses and sphincteric disturbances appear much earlier than in syringomyelia, and the syndrome of Froin (yellow cerebrospinal fluid very rich in protein and undergoing spontaneous coagulation in the test-tube) is often present.

The resemblance between *leprosy* and syringomyelia may also be close, but early involvement of the nasopharynx, discoloration of the skin, implication of the upper branches of the facial nerve, an irregular patchy distribution of anesthesia over the trunk and all four extremities, osteoporotic bone changes and an absence of scoliosis, of muscular twitchings, of intensified tendon reflexes, of spastic phenomena in the legs, and of muscular atrophy in the arms speak against syringomyelia. In obscure cases the finding of the lepra bacillus or even of nodular swellings in the nerves will be decisive. In *arteriosclerotic changes*, with sensory and trophic disturbances, dissociation of sensation is absent and signs of impaired circulation in the affected vessels are usually apparent. *Raynaud's disease* is distinguished by absence of partial paralysis of sensation, muscular atrophy, spastic phenomena, scoliosis, bulbar symptoms, painless joint affections, etc. *Cervical rib* sometimes produces symptoms suggestive of syringomyelia and occasionally the two conditions coexist in the same patient.

**Prognosis and Treatment.**—The disease is incurable, but its progress is slow, often extending over many years and periods of temporary improvement are not uncommon. Even the occurrence of bulbar symptoms may not materially hasten the end. The treatment is purely symptomatic.

## TUMORS AFFECTING THE SPINAL CORD

Tumors affecting the spinal cord are comparatively rare. Schlesinger[1] found only 151 in 35,000 necropsies, or one-sixth as many as brain tumors. More than three-fourths of the cases occur between the ages of 15 and 50 years. Any portion of the vertebral column or spinal cord may be affected, but the greatest number of tumors occur in the thoracic region. The posterior aspect is a much more favorite site than the anterior.

**Varieties.**—Spinal tumors may be divided into those arising from the vertebræ and those arising from the cord and its membranes. Intravertebral growths are further divided into extramedullary and intramedullary. Tumors of the vertebræ are more than twice as common as those of the meninges and of the cord combined. Of 400 cases of intravertebral growths collected by Schlesinger, 239 were extramedullary and 126 were intramedullary. Of the 239 extramedullary growths 88 were extradural and 151 were intradural. Nearly a third of the entire number were multiple. Of 67 spinal tumors operated upon by Elsberg[2] almost 75 per cent. were extramedullary. The large majority of vertebral new growths are metastatic, carcinoma being more common than sarcoma. On the other hand, primary tumors of the meninges and cord are more common than secondary metastatic growths. The chief intravertebral growths are endothelioma, psammoma, glioma, fibroma, tubercle, and gumma. Endothelioma, psammoma, fibroma and gumma are, as a rule, extramedullary (meningeal). Tuberculoma occurs as a focal meningo-myelitis or as a solitary tubercle of the cord itself. Glioma is always intramedullary and is usually diffuse. It is by far the most common of the true neoplasms developing within the substance of the spinal cord.

**Symptoms.**—The symptoms vary in character and in the order of their development according to the position and the consistence of the tumor. Neuralgic pain, due to irritation of the nerve roots, is usually the earliest manifestation when the growth develops in the *vertebræ*. The pain is referred to a segmental skin area and is often for a time unilateral. The painful areas are usually hyperesthetic, but the nerve-trunks themselves are not tender upon pressure. Local tenderness and a rounded kyphosis are frequently observed at the site of the growth. Following the neuralgic period, motor and sensory paralysis in parts supplied by the cord below the level of the lesion develop gradually or sometimes abruptly. The motor palsy is at first spastic, but with complete destruction of the conductivity of the cord it becomes flaccid. The sphincters are sooner or later affected and in advanced cases bedsores supervene. The impairment of sensibility usually involves all forms of sensation, but not always in the same degree. Occasionally there is well-marked dissociation anesthesia. More or less asymmetry in both the motor and sensory paralysis is not uncommon and in some cases the picture of Brown-Séquard's paralysis[3] is produced.

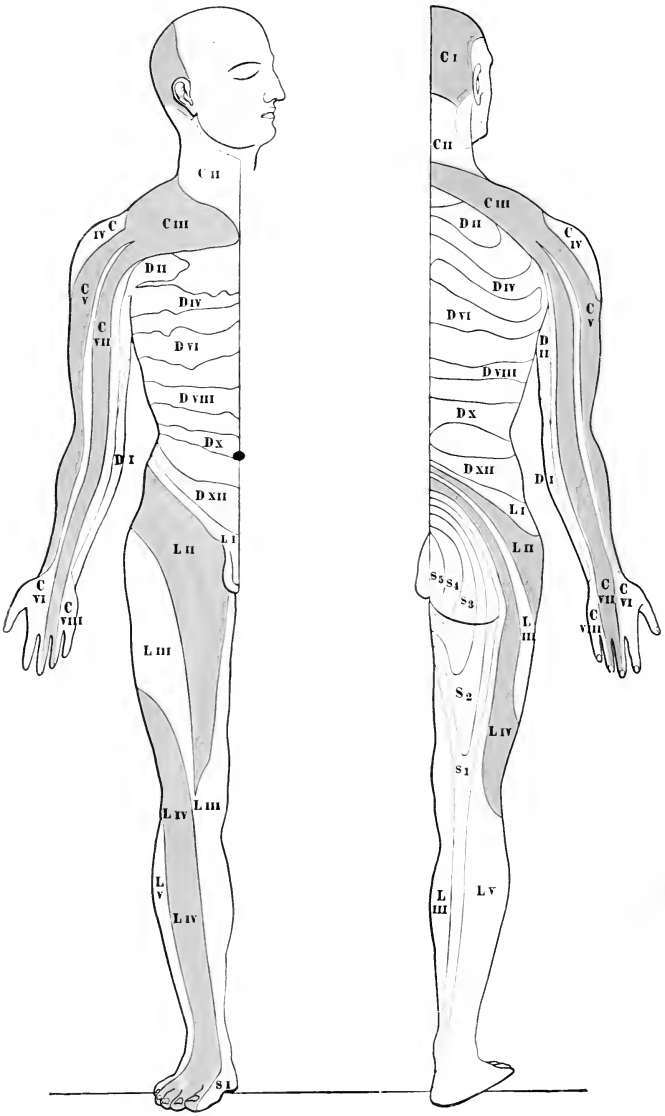
*Extramedullary (meningeal) tumors*, as a rule, also present neuralgic pains for a variable period. With the growth of the tumor, signs of compression of the cord make their appearance. Both the motor and sensory paralysis may for a time be unilateral or more pronounced on one side than on the other. The upper boundary of sensory disturbance is usually horizontal and remains virtually in the same place on the trunk throughout the illness. The paralysis may remain spastic for many months. Vertebral

[1] Schlesinger: Rückenmarkstum, Jena, 1898.

[2] Amer. Jour. Med. Sci., Feb., 1920.

[3] Motor paralysis on the side of the lesion with anesthesia at the level of the lesion on the same side and below the level of the lesion on the opposite side of the body.

PLATE I




Areas of anesthesia upon the body after lesions in the various segments of the spinal cord. The segments of the cord are numbered: C I to VIII, D I to XII, L I to V, S 1 to 5, and these numbers are placed on the region of the skin supplied by the sensory nerves of the corresponding segment (Starr).

symptoms, such as localized pain, tenderness and kyphosis are usually absent.

In *intramedullary tumors* neuralgic pains are, as a rule, wanting or are mild and transitory, the outstanding feature being a progressive loss of motor power, of pain, tactile, and temperature sensibilities, and of reflexes in the segments at the tumor level, together with an exaggeration of the reflexes below the tumor level. The Brown-Séquard type of paralysis may be observed, but it is transitory. In contrast with meningeal tumors, the upper boundary of sensory disturbance often moves upward as well as downward owing to the marked tendency of intramedullary tumors (gliomata) to infiltrate the cord in both directions.

The **duration** of spinal tumors varies from a few months to several years. Generally speaking it is shortest in malignant vertebral growths and longest in extramedullary psammomas.

**Diagnosis.**—This may be difficult, especially if there is no evidence of a primary growth in any other part of the body and the neoplasm is an intramedullary one. *X*-ray examination is not usually helpful except in vertebral tumors. Examination of the cerebrospinal fluid may be negative, but not infrequently it reveals the syndrome of Froin[1] which consists of xanthochromia, spontaneous coagulation and an increase in the cell count. This syndrome, especially if complete, is suggestive of compression of the cord, but is not conclusive evidence of tumor. Other investigators have shown that compression is indicated also by a marked increase in protein and a low cell count, with or without xanthochromia (Nonne,[2] Raven, Ayer[3] and Viets[4]) The conditions most likely to be confused with spinal tumor are tuberculous spondylitis (Pott's disease), syringomyelia, disseminated sclerosis, pachymeningitis cervicalis, and circumscribed serous meningitis. In *Pott's disease*, the pain is usually less severe and more symmetrical, the rigidity of the spine is, as a rule, more pronounced, the deformity is more angular, cold abscesses are frequently present, the course is less rapid, and the x-ray evidence is often conclusive. *Syringomyelia* can usually be distinguished by the presence of muscular atrophy, dissociated disturbances of sensation, trophic changes in the bones, joints and skin, and the protracted course. *Disseminated sclerosis* is distinguished by the absence of pronounced and persistent sensory phenomena, by the presence of nystagmus, intention tremor, scanning speech, optic atrophy, etc., and by a slow course, often marked by remissions and exacerbations. *Pachymeningitis cervicalis* may at first closely simulate spinal tumor, but eventually the prolonged course, the muscular atrophy, and the peculiar position of the hands and fingers will point the way to the diagnosis. *Circumscribed (cystic) serous* meningitis produces the symptoms of a slowly developing tumor and cannot be distinguished with certainty without recourse to exploratory laminectomy. Oppenheim and Krause[5] found it in 6 of 21 laminectomies and Adson[6] in 3 of 16 laminectomies.

As regards the *location of the tumor*, the upper limit of sensory disturbance usually gives the clue, the spinal cord segment to which the affected cutaneous region belongs being determined with the aid of the well-known diagrammatic schemes of Edinger and others.

**Treatment.**—Except in gummata, prompt surgical intervention affords about the only hope of cure. In a case reported by Weisenburg and in one

[1] Gaz. d. Hôp., 1903, lxxxvi, 1005.
[2] Deutsch. Zeitsch. f. Nervenh., 1910, xl, 161.
[3] Deutsch. Zeitsch. f. Nervenh., 1912, xliv, 380.
[4] Jour. Amer. Med. Assoc., 1916, lxvii, 1707.
[5] Quoted by Ewing, "Neoplastic Diseases," Phila., 1919, p. 426.
[6] Jour. Amer. Med. Assoc., 1920, lxxv, 1132.

reported by Sachs complete relief resulted from lumbar puncture. The mortality in 67 cases treated surgically by Elsberg[1] was 10.4 per cent. In a group of 330 surgical cases reviewed by Frazier[2] 18 per cent. were cured completely and 19 per cent. were improved. Redlich[3] reports 21 operative cases, with complete cure in 5 of the 8 extramedullary tumors and in 3 of 7 cauda tumors; marked improvement in 2 cases and slight improvement in 1 case.

### TUMORS AFFECTING THE CAUDA EQUINA

Tumors affecting the lumbosacral roots usually spring from the vertebræ or an intrapelvic structure, although they may have their origin in the cauda equina itself. Stiffness in the lumbar region and pain extending down the posterior aspect of one thigh and then of other thigh (sciatica) are usually the first symptoms. The pain at first is often intermittent. Later, weakness of the peroneal muscles with dropfoot occurs, the knee- and ankle-jerks disappear, the vesical and rectal sphincters become affected, and hypesthesia develops in the perineum and genitals and around the anus. Lumbar puncture may yield no fluid. Physical examination of the lower vertebræ and sacrum and of the pelvis by way of the rectum or vagina may yield important information. Local tenderness of the spine is not uncommon. Occasionally, there is edema of the legs. In many cases the patient has been treated for long periods for ordinary sciatica or tabes. In *lesions of the conus* the symptoms usually develop more rapidly, pain is commonly less conspicuous and may be absent, anesthesia often appears simultaneously with the motor paralysis and is not rarely of a dissociative type, the power of erection and ejaculation may persist even with complete paralysis of the bladder and rectum, and decubitus is more likely to occur. Spastic paralysis with persistent increase of the reflexes is decidedly opposed to caudal disease. In *multiple neuritis* the history of alcoholism or of a previous infection is usually obtainable, the nerve-trunks are tender upon pressure, and the sphincters are rarely affected. *Hypertrophic arthritis* of the *lumbar spine* and *tuberculosis of the sacrum* may usually be excluded by roentgenography. Thus far surgical intervention has been somewhat unsatisfactory.

## HYPERKINETIC DISEASES

### INFECTIOUS CHOREA

**(Sydenham's Chorea; Chorea Minor; St. Vitus' Dance)**

**Definition.**—Infectious chorea is a relatively common disease, occurring principally in childhood and adolescence, probably due to the action of bacterial toxins on the central nervous system, and characterized by brief involuntary muscular contractions of a disorderly and purposeless nature,

[1] Amer. Jour. Med. Sci., Feb., 1920.
[2] Frazier: "Surgery of the Spine and Spinal Cord," 1918, New York.
[3] Medizin. Klin., 1921, No. 44.

more or less psychic disturbance, and a pronounced tendency to endocarditis.[1]

**Etiology.**—Chorea is ordinarily a disease of childhood and adolescence, about four-fifths of the cases occurring between the age of 5 and 15. However, it may develop at any age, even in the extremes of life. Females are affected more frequently than males, the ratio in the two sexes being about 2 to 1. The disease is more prevalent in the spring months than at any other season of the year. Neuropathic heredity plays a definite but by no means a dominant rôle. Quite as important as heredity are habits of life which tend to exhaust the nervous system or render it abnormally irritable. That a close relationship exists between chorea and rheumatism has been clearly established, but before the view held by many English and Continental authorities that all cases are rheumatic can be accepted, much experimental work needs to be done to determine the etiology of rheumatism itself. Moreover, as there is no concensus of opinion among clinicians as to what really constitutes rheumatism, it is difficult to state definitely in what proportion of cases chorea is attended or preceded by that disease. From 20 to 30 per cent. is probably a fair estimate, but if all the vague muscular pains of childhood are regarded as rheumatic, this proportion will be found much too low. Occasionally, chorea follows immediately upon one of the other acute infections, especially scarlet fever.

In many cases the jerking movements first appear while the child is under some depressing emotion, such as fright or grief. Nervous shock, however, is probably never the sole etiologic factor, for it is inconceivable that a disease so frequently attended by vegetative endocarditis, as chorea, could be brought into existence by a mere psychic disturbance. Somewhat similarly, the acute symptoms of alcoholism (delirium tremens) or of uremia are often evoked by the action of apparently slight external causes upon a system already impregnated with the respective poison.

Much stress has been laid by some authors upon peripheral irritation, as from intestinal worms, phimosis, eye-strain, etc., but while this seems to be capable of producing certain tic-like contractions, it probably plays little, if any, part in the etiology of true chorea.

In females after the age of puberty, pregnancy has some predisposing influence. The disease occurs most frequently in young primiparæ and usually develops during the first six months of gestation. In 40 cases of chorea gravidarum observed by Wall and Andrews[2] at the London Hospital there was a history of previous chorea in 23 and of previous rheumatism in 16.

**Morbid Anatomy and Pathogenesis.**—As death is uncommon in simple chorea opportunity to study the pathology of the disease is not often afforded. The lesions reported have been found chiefly in the brain and have consisted of perivascular round-cell infiltration, some thickening of the vessel walls, small hemorrhages, chromatolysis within the nerve-cells, and the appearance of globular structureless bodies somewhat resembling corpora amylacea (*Choreakörperchen*). These changes were most pronounced, as a rule, in the motor tracts and basal ganglia. In a case recently studied by Marie and Tretiakoff[3] the putamen and caudate nucleus of the corpus striatum and

[1] The term *chorea Sancti Viti* was originally applied to the dancing mania, a form of hysteria, prevalent in Europe during the fifteenth and sixteenth centuries, and for the cure of which pilgrimages were made to various shrines, particularly that of St. Vitus, a young Sicilian who suffered martyrdom in the time of Diocletian. Later, Sydenham gave the name of chorea to the infection now under consideration. Much confusion arose from this new use of the term and in consequence the dancing mania became known as *chorea magna* and the disease described by Sydenham as *chorea minor* or *chorea anglorum*.

[2] Jour. of Obstet. and Gynecol. of Brit. Empire, June, 1903.

[3] Rev. Neurol., 1920, xxvii, 428.

the cortex of the cerebrum were especially affected. In addition, slight leptomeningitis and multiple capillary emboli have been noted in isolated cases. A number of observers have also demonstrated diplococci or streptococci in the cerebral tissues (Pianese, Triboulet, Dana, Meyer, Geddes and Clinch, Griffith, and Poynton and Holmes).

The *pathogenesis* of chorea is obscure. The seasonal prevalence of the disease, its self limitation, the occurrence of vegetative endocarditis in many cases, and the character of the changes observed post-mortem all point to an infectious origin.

On the other hand, the peculiar conditions under which so many of the attacks occur seem to indicate that abnormal irritability of the nervous system is an important factor in determining the direction in which some of the force of the infectious process shall expend itself. Whether the infecting agent is always the same or may be different in different cases is a question to which no positive answer can be given at the present time.

**Symptoms.**—The onset may be abrupt, but more frequently it is gradual and preceded by a short prodromal period marked by depression, peevishness, and disturbed digestion. The first conspicuous symptoms are usually restlessness, awkwardness in movement, and nervous irritability, so that not rarely the child is punished for being fidgety. As the disease advances true choreic movements make their appearance. These are involuntary, purposeless, jerky, and bizarre. They may involve every voluntary muscle of the body, but, as a rule, the face and extremities are chiefly affected. Not rarely the contractions are confined to one part or to one side of the body (hemichorea). When the facial muscles are involved the most varied expressions and grimaces are produced. When the upper extremities are affected the shoulders are alternately raised and lowered, the arms pronated and supinated, and the fingers flexed and extended, or otherwise moved. In severe cases the movements of the arms may be so uncontrollable that it is impossible for the patient to dress or feed himself, to write, or to perform any act requiring a high degree of coördination. When the legs are implicated constant changes of position occur while the patient is at rest, and walking is interfered with or rendered impossible. Chorea of the pharyngeal muscles is manifested by difficulty in deglutition and of the laryngeal muscles by indistinct explosive articulation or complete inability to utter intelligible sounds. In some cases, owing to the participation of the thoracic muscles and diaphragm in the involuntary contractions, irregularities of the respiratory rhythm are observed.

Occasionally, the movements are so general, so constant and so furious that the patient must be strapped in bed to prevent him from falling out, and even with the utmost care contusions and extensive excoriations occur.

The choreic movements become less marked during repose and, except in severe forms of the disease, cease entirely during sleep. Unless intense, they cause little or no fatigue. Although the choreic patient is always awkward and frequently drops objects from his hands, he does not usually show any conspicuous loss of motor power. As a matter of fact, however, slight weakness is nearly always present in the affected muscles and occasionally the paresis is so pronounced that it overshadows the motor excitation and thus leads to error in diagnosis. The reflex activity may be diminished or exaggerated. Inequaliy of the pupils, rhythmic oscillations of the iris (hippus), and an abnormally rapid contraction of the pupils both to light and to accommodation are sometimes observed, but are not significant.

Sensibility is not affected, but articular and muscular pains, usually of a rheumatic character, are often complained of. Next to the motor manifesta-

tions the most constant feature of the disease is the psychic change. This is manifested as a rule, merely by fretfulness, irritability, moodiness, some loss of power of fixing the attention, weakness of memory, and impairment of volition. Less frequently there are also transitory hallucinations, and occasionally, in severe cases, the mental disturbance is pronounced, showing itself as a confusional condition or as actual delirium. Psychic changes of one kind or another were observed in 827 of Starr's[1] 1400 cases.

Some impairment of the general health with loss of weight is common. A mild grade of chlorotic anemia is not infrequently observed. Various microörganisms have been isolated from the blood in malignant cases. Even in mild attacks there is often at times slight fever and in grave forms of the disease the temperature may rise to 103 or 104° F. The urine rarely shows any decided abnormalities, but glycosuria and hematoporphyrinuria have been observed in a few instances. The cerebrospinal fluid is clear and sterile and sometimes shows a slight pleocytosis of the mononuclear type (Morse and Floyd[2]).

**Forms.**—Between the *mild* attacks in which momentary contractions of a few muscles and nervous irritability are the only symptoms and the comparatively rare *malignant* forms characterized by incessant writhings of the entire body, with fever, and perhaps delirium (*chorea insaniens*), there is every gradation. When the involuntary movements are attended by actual paresis of the extremities the condition is termed *paralytic chorea*. Care must be taken, however, to distinguish between true motor weakness and pseudo-paresis dependent on defective coördination. The possibility of actual paresis being caused by the long continued use of arsenic (arsenical neuritis) as a remedy must also be considered in some cases.

**Complications.**—*Endocarditis* is the most important complication, both the valvular disease and the disturbance of the central nervous system being the result of the same original cause. Of 140 patients examined by Osler more than 2 years after an attack of chorea, 72 (51.4) presented evidences of organic heart disease. Thirty-two per cent. of the 439 cases studied by the Committee of the British Medical Association[3] and 31 per cent. of the 226 cases analyzed by Abt and Levinson[4] showed cardiac involvement. The endocarditis is usually of the warty or benign form and shows a strong predilection for the mitral valve. *Pericarditis* is an occasional complication. The usual indications of coincident *rheumatism* are present in from 5 to 10 per cent. of the cases.

**Diagnosis.**—Choreiform movements must be distinguished from tremors, motor tics, localized spasms, the myocloniæ of the Friedreich, Dubini and Henoch types, and athetosis. *Tremors* are involuntary to-and-fro movements of slight extent, produced by the rhythmic contraction of antagonistic muscles. In contrast with tremors choreiform movements are non-vibratory, quickly changing, and of wide range. In the *motor tics* the movements are such as normal persons often execute. Although performed for no purpose, they are natural and are pathologic only in their inopportuness, involuntary reproduction and frequency of repetition. In tic the same movement is repeated over and over again, while in chorea the movements are ever changing. Further the movements of tic, unlike those of chorea, are never disabling, and can be controlled, at least for a short time, by the will. The *localized spasms* most likely to be confused with choreiform movements

[1] Jacobi Festschrift, 1900, 5.
[2] Amer. Jour. of Dis. of Child., July, 1916.
[3] Brit. Med. Jour., 1887, i, 425.
[4] Jour. Amer. Med. Assoc., Nov. 4, 1916.

are those affecting the face. In facial spasm, however, the convulsive movements are always the same, are strictly limited to the area of distribution of the facial nerve, and are often continued during sleep. In *myoclonia of the Friedreich, Dubini and Henoch types,* the contractions are rhythmical, abrupt and rapid, as if produced by an electric shock. *Athetosis* is most frequently met with as an accompaniment of spastic hemiplegia or diplegia of infancy. The movements, which affect chiefly the fingers and toes, are slower, more rhythmical, and more consecutive than those of chorea.

Once involuntary movements are recognized as being definitely choreiform there is rarely any difficulty in deciding whether they are due to infectious chorea or some other condition. *Huntington's chorea* is almost always hereditary and familial; it is a disease of adult life; it develops gradually and is progressive; and it tends to insanity. Choreiform movements occurring in focal brain disease (*post-hemiplegic chorea*) are not likely to be mistaken for those of infectious chorea unless the paralysis is ill-defined. The history of the onset and the spastic rigidity of the muscles will usually make the diagnosis clear. *Senile chorea*, the result of widespread cerebral arteriosclerosis, rarely gives rise to confusion. In 55 cases on record analyzed by Eichhorst[1] the chorea was chronic in 49 per cent., the movements were unilateral in 23.6 per cent., and there was more or less mental disturbance in 43.6 per cent. The *choreiform movements of hysteria* simulate more or less closely those of infectious chorea, but the former are usually more rhythmical than the latter and are accompanied by other stigmata of hysteria. The fact must not be forgotten, however, that the two conditions occasionally coexist in the same patient.

**Course.**—As regards life the prognosis is good. The mortality is probably not more than 2 per cent. It should be remembered, however, that relapses are common and that cardiac complications occur in more than 25 per cent. of the cases. The duration of the disease varies. In the majority of cases it is from 6 to 12 weeks, but occasionally the movements continue for a year or more. The relapses usually occur at the same period of the year at which the primary attack developed, and many patients suffer from 3 or 4 attacks. Movements so violent as to interfere with sleep, high fever, and delirium determine a guarded prognosis. Chorea gravidarum is not in itself especially unfavorable when the pregnancy is otherwise uncomplicated. While some writers (Fehling, Oppenheim, Gowers) state the mortality is between 20 and 30 per cent., Wall and Andrews report 28 cases with 2 deaths and Shaw[2] 32 cases with no deaths.

**Treatment.**—Rest of body and mind is the most important factor in the treatment of the disease. No matter how mild the attack, the child should be taken from school. If the symptoms are at all severe rest in bed in a quiet, well-ventilated room should be insisted upon, the bed being well padded on all sides to prevent the patient from injuring himself. To insure complete repose it is often necessary to exclude the child's playmates and even his own brothers and sisters from the room. The diet should be liberal and nutritious.

Gentle massage is sometimes beneficial, especially in poorly nourished children, but no gymnastic exercises should be allowed until convalescence is firmly established. Prolonged warm baths, the temperature of the water being maintained at about 95° F. (35° C.) are often decidedly helpful. Two such baths may be given during the day. In older children, especially in highly neurotic cases, the wet pack may be used with advantage. A change

[1] Med. Klinik, 1911, No. 7.
[2] Brit. Med. Jour., Jan. 24, 1914.

of air, especially a change to the seashore, is of benefit in mild but refractory cases. On account of the marked tendency to relapse, children who have once suffered from the disease should not be overtaxed at school and should be guarded, as far as possible, from attacks of rheumatism.

The employment of drugs is of secondary importance. Arsenic has been extensively used, but its value is at least doubtful. A child of 5 or 6 years may be given as an initial dose 3 minims (0.2 mil) of Fowler's solution three times a day, and this amount may be gradually increased by a minim a day until 10 minims (0.6 mil), three times a day, are being taken. If puffiness about the eyes, nausea, intestinal colic, or diarrhea occurs the administration of the drug should be suspended for several days and then resumed at a dose somewhat less than the child was taking when the untoward symptom appeared. Arsenic should always be given after meals and well diluted. While taking large doses the patient should be kept under close observation, as albuminuria, conjunctivitis, inflammatory diseases of the skin or even neuritis may develop independently of the usual untoward effects.

Antipyrin in doses of 15 to 20 grains (1.0–1.3 gm.) a day, at six years of age, has been advocated by a number of writers, but when used so freely this drug may cause cyanosis, anemia, and prostration. Salicylates are of service when rheumatism occurs in association with chorea, otherwise they usually fail. Autoserum treatment, originally proposed by A. Goodman,[1] and consisting in withdrawing blood (50 mils) from the patient, separating the serum, and injecting 15 to 20 mils of this into the spinal canal after removing an equal amount of cerebrospinal fluid, has not proved uniformly successful. In a recent report, however, Brown, Smith and Phillips[2] claim far better results from it than from any other method of treatment. In the 23 cases cited a cure was obtained within 3 weeks in 77 per cent. and improvement in 19 per cent. The average number of injections was three. It is important that all drug therapy be suspended before the treatment is begun.

When the movements are violent and interfere with sleep recourse must be had to sedatives. The best are chloral, bromids, luminal and trional. Morphin is rarely indicated. In addition to special medicaments and sedatives, iron is often required to combat anemia.

In chorea insaniens hyoscin hypodermically, in doses of $\frac{1}{200}$–$\frac{1}{100}$ of a grain (0.0003–0.0006 gm.) twice daily, sometimes acts well. Inhalations of chloroform may be necessary. Forced feeding is occasionally imperative. Cases of chorea complicating pregnancy call for a diet limited to milk and diluents and a systematic eliminative treatment by cathartics, diuredtics and diaphoretics. The induction of abortion or premature labor is rarely necessary.

## HUNTINGTON'S CHOREA

### (Chronic Hereditary Chorea)

Huntington's chorea is an hereditary affection usually developing in adult life, characterized by general choreiform movements, and mental deterioration, and pursuing a chronic progressive course.

This comparatively rare disease was recognized by Waters[3] as early as

[1] Arch. of Pediat., 1916, xxxiii, 649.
[2] Brit. Jour. of Child. Dis., 1919, xvi, 8.
[3] Practice of Medicine: Dunglison, 1848.

1841, but it was first fully described by Huntington[1] in 1872. It usually makes its appearance between the ages of 35 and 40 years, although occasionally it begins in childhood. In the vast majority of cases it is directly handed down from one generation to another. As a rule, if one member of a family escapes his descendants also have immunity. Occasionally, cases are observed in which heredity is not a factor. The pathology of the disease is still undetermined. Various changes, such as atrophy of the gyri, proliferation of the neuroglia, and signs of cortical encephalitis, especially of the motor cortex, have been described. According to Marie and Lhermitte[2] the essential lesion is a degenerative atrophy of the cerebral cortex and striate body. J. R. Hunt[3] accepts the view that the striate body is a motor

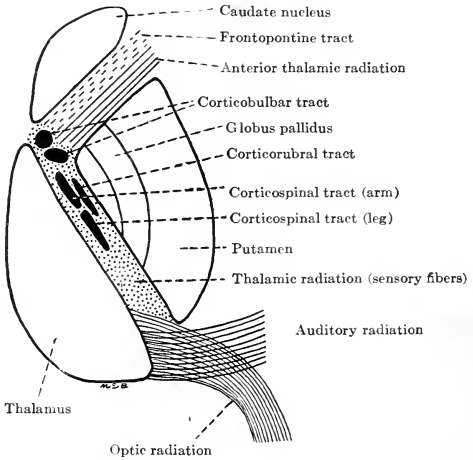



FIG. 35.—Diagram of the internal capsule (Ranson).

mechanism for the control of automatic and associated movements operating through the extrapyramidal motor tracts, and believes that atrophy of the large motor cells (pallidal) is responsible for paralysis agitans and atrophy of the smaller cells in the caudate and putamen is responsible for Huntington's chorea.

**Symptoms.**—The movements at first slight and confined to the upper extremities and face, gradually increase in intensity and become more general, until at least the voluntary muscles of the entire body, except those of the eyes, are affected. As a rule, the movements are of wider range, more extensive, more deliberate and more clown-like than those of infectious chorea. The gait is characteristic. After several natural steps, one foot is thrown forward making a long stride and then in a measured way, as in dancing, the other is brought up to the first. A drawling, hesitating speech and peculiar grimaces and gestures also form an important part of the clinical picture. Mental disability is rarely absent. It may be present from the

[1] Med. and Surg. Reporter, April 13, 1878.
[2] Annal. de Méd., 1914, No. 1.
[3] Jour. Amer. Assoc., June 23, 1917.

onset but, as a rule, it does not show itself until the patient has been choreic for several years. The usual mental state is one of depression with delusions of persecution and a tendency to suicide Eventually, there may be complete dementia. The disease is incurable but of slow course, a duration of 20 or even of 30 years being not uncommon.

## PARALYSIS AGITANS

### (Shaking Palsy; Parkinson's Disease)

**Definition.**—Paralysis agitans is a chronic progressive disease of the nervous system characterized by permanent muscular rigidity and lengthening of the reaction-time of the muscles to auto-stimulation, which phenomena result in peculiar changes in posture, gait, facial expression and speech, and which are usually associated with a characteristic tremor, gradually increasing in extent and intensity.

The disease, first accurately depicted by Parkinson[1] in 1817, is relatively uncommon, comprising scarcely more than 1 per cent. of the whole number of cases seen in a general clinic for nervous affections.

**Etiology.**—This is imperfectly understood. The disease usually develops (three-fourths of the cases) in the presenile period between the 45th and 65th years and is rare before the 30th or after the 70th year. In 1911 Willige[2] collected from the literature 47 cases in persons under 30 years of age, including 12 under 20. Men are attacked more frequently than women, the proportion being about 3 to 2. Heredity and a neuropathic disposition are of subordinate importance. Neither syphilis nor alcoholism plays any rôle. Numerous observations have demonstrated beyond doubt that emotional or psychical shock—fright, anxiety, grief or anger—may be an important provocative factor. In a small proportion of cases a causal connection between physical trauma and the onset of the disease can be unmistakably established and under these circumstances the member that has sustained the injury is usually the seat of the earliest symptoms. Exposure to cold, overwork, and infectious diseases have also been mentioned as exciting causes, but apparently on no very good grounds. Occasionally, paralysis agitans develops as a sequel of epidemic encephalitis.

**Morbid Anatomy.**—Of the pathology of paralysis agitans nothing definite is known. Koller, Redlich, Gordinier and others have found sclerotic changes in the bloodvessels, glia proliferation, and pigmentation and atrophy of the nerve cells, especially in the spinal cord. These findings are similar to those commonly observed in the nervous system of the aged and it is well recognized that the most marked senile changes may be present without the occurrence of paralysis agitans; nevertheless, some writers look upon the disease as an expression of an intense, but premature, form of senility.

Camp[3] found in all of 9 cases the anomalies in the muscles, especially the pathologic changes in the muscle spindles, previously described by Schiefferdecker and Schultze.[4] As these bodies apparently exert an influence on muscle tonus, and as the symptoms of paralysis agitans usually begin in muscles most abundantly supplied with spindles and spare those which contain

[1] Essay on the Shaking Palsy, London, 1817.
[2] Zeitsch. f. d. ges. Neur. u. Psych., 1911.
[3] Jour. Amer. Med. Assoc., April 13, 1907.
[4] Deutsch. Zeit. f. Nervenkeilk., Dec., 1903.

none, the view has been advanced that the muscle spindles are the seat of the morbid process. Camp, while admitting that the muscle changes may be due to premature decay (abiotrophy), favors the view that they are caused by a general toxemia, possibly the result of an alteration in the parathyroid glands.

Recent studies of the lesions in Wilson's disease (progressive lenticular degeneration), which has several features in common with paralysis agitans, have drawn attention to the lenticular nucleus of the striate body as the site of the causal lesion. J. Ramsey Hunt has found definite alterations of an atrophic or degenerative character in the large motor cells (pallidal cells) of the lenticular nucleus. He accepts the view that the striate body is a motor mechanism for the control of automatic and associated movements operating through the extrapyramidal motor tracts and believes that paralysis agitans is a systemic disease of the striaspinal mechanism while primary lateral sclerosis is a systemic disease of the corticospinal mechanism.

**Symptoms.**—The disease usually develops insidiously, although it may come on suddenly. The first complaint may be of general lassitude, rheumatoid pains, and headache, or of a sense of unwieldiness or fatigue in the limb in which the characteristic symptoms—tremor and muscular rigidity—subsequently manifest themselves. In the majority of cases, however, *tremor* is the first symptom for which the patient seeks relief. The part attacked is, as a rule, one of the hands, where in addition to the oscillations, there is often to be seen a movement of the thumb over the other fingers similar to that produced in rolling a pill or crumbling a morsel of bread. The trembling, which for a time is usually intermittent, gradually spreads to the rest of the limb and sooner or later appears somewhere else, most frequently in the leg of the same side. Finally, all of the limbs and even the head may be affected. Nystagmus, however, is never observed. The tremor is relatively slow (5 or 6 oscillations to the second), persists during repose, is augmented by mental excitement, and ceases, as a rule, during sleep. Usually, but not invariably, it is lessened in intensity by purposeful movements. Occasionally, tremor is absent from first to last.

Another striking phenomenon of the disease is *muscular rigidity*, which is responsible for the peculiar changes in the attitude and facial expression. The head and body are usually inclined forward, the arms are slightly bent at the elbow and the legs at the knee, and the three inner fingers are flexed and often turned toward the ulnar side, as in arthritis deformans, while the thumb and forefinger are brought close together as in holding a pen. Rarely an "extension type" is observed in which the head and trunk are inclined backward, rather than forward. The *facies* is characteristic. The eyes are staring and fixed, winking is infrequent, the surface is smooth, and the features are peculiarly unresponsive to the emotions ("mask face").

Partly as a result of the muscular rigidity and partly as a result of the lengthening of the reaction-time of the muscles to auto-stimulation, nearly all purposive movements are both begun and arrested with difficulty. This is often well shown in the *gait*. The patient, if seated, rises slowly, then steadies himself for a few seconds, and at length, after having made a few shuffling steps, shows an almost irresistible tendency to hurry ahead and to fall forward (propulsion or festination). Occasionally there is a tendency to walk or fall backward (retropulsion) or toward one or the other side (lateropulsion). Whatever the direction of the movement, it may often be reversed by gently pulling at the patient's clothing. Among other symptoms having the same significance may be mentioned the tardiness with which voluntarily induced wrinkling of the forehead disappears upon forced attempts

to remove it and the ever-present difficulty in changing the direction of the eyeballs (lateropulsion oculaire). Although there is no actual impairment of articulation, the speech is often slow and jerky, the voice piping and monotonous.

Among other symptoms more or less frequently observed are a subjective sensation of excessive heat in various parts of the body, a feeling of extreme fatigue in the muscles, cramps in the legs, outbreaks of sweat, and attacks of sialorrhea. Intense restlessness with a desire for frequent changes of position is also noted in many cases. Objective disturbances in sensibility are absent, intelligence is unimpaired, the reflexes are, as a rule, undisturbed, the sphincters are intact, and the vegetative functions are normal.

**Course.**—Recovery probably never occurs and remissions are rare, but the course of the disease is slow, twenty or thirty years often elapsing before the final stage is reached. Ultimately, complete helplessness supervenes and the patient becomes bedridden. Death is usually the result of some intercurrent affection, especially pneumonia.

**Diagnosis.**—Well developed cases of paralysis agitans in its typical form may be recognized at a glance. Even when the tremor is absent, the muscular stiffness, blank expression, slow movements, and peculiar gait will usually suffice to remove at once all doubt as to the true condition. In the early stages of the disease, however, the diagnosis is not always easy, especially as a long period may intervene between the appearance of the first vague symptoms and the development of the distinctive features. The differential diagnosis from other forms of tremor is not usually difficult. In the tremor of *senility* the head is especially affected and the other cardinal symptoms of paralysis agitans are absent. In *alcoholism* the history and appearance of the patient are suggestive, the tremor usually decreases in intensity under the influence of stimulants, and muscular rigidity with its characteristic sequelæ is lacking. The tremor of *hysteria* is generally of wider range, presents greater variations, and shows more tendency to involve the proximal part of the limbs than that of paralysis agitans. Moreover, it is nearly always accompanied by other stigmata of hysteria and is not attended with muscular rigidity and its peculiar consequences. The tremor of *disseminated sclerosis* appears only when voluntary movements are undertaken and is associated with other symptoms foreign to paralysis agitans, such as nystagmus, paresis of the ocular muscles, visual defects, pallor of one or both optic discs, ankle clonus, scanning speech, disorders of micturition, psychic alterations and emotional outbreaks.

*Progressive lenticular degeneration* (*Wilson's disease*) is also characterized by tremor, increased muscular tonicity, facial immobility, but the tremor is always increased when voluntary movements are attempted, the muscular hypertonicity is so intense that it results in contractures and malposition in the extremities, and the facial expression is stupid or even idiotic. Moreover, progressive lenticular degeneration is essentially a disease of childhood or adolescence, and is often familial.

Neither *family tremor* nor the tremor of *hyperthyroidism* is likely to cause confusion.

The differential diagnosis of slowly developing *hemiplegia* of organic origin from the unilateral form of paralysis agitans, while not usually perplexing, may at times occasion great or insurmountable difficulty. In their later phases *bulbar palsy* and paralysis agitans may resemble one another. Indeed, the two diseases occasionally coexist in the same patient. This is also true of *arthritis deformans* and paralysis agitans, between which, strange to say, there is sometimes a close resemblance.

**Treatment.**—Although paralysis agitans is incurable, much can be done to alleviate the symptoms and make the patient more comfortable. A life free from worry and excitement, in a congenial environment, and varied by change of climate in the trying seasons of the year is one which best meets the requirements. While the expenditure of energy should be restricted and an abundance of sleep is always necessary, rest-treatment is contraindicated. Lukewarm baths, continued for 10 or 15 minutes, and combined with passive movements and active, but gentle, exercises, may do much toward relaxing the muscular rigidity and overcoming the physical inertia. Swift[1] reports favorable results from simple muscular movements of the different members successively, performed very slowly at the rate of about one foot to the second, with strong mental concentration upon the movement while it is in progress. Vibration, such as is produced by riding in a railway train, sometimes affords considerable comfort. Massage and electricity, however, are of doubtful value. Tonics, especially arsenic and iron, may often be used with benefit. Strychnin is contraindicated. Among the numerous sedatives extolled for their favorable effect upon the tremor, the best is undoubtedly hyoscin hydrobromid. From $\frac{1}{200}$ to $\frac{1}{100}$ of a grain (0.0003–0.0006 gm.) may be given, preferably hypodermically, two or three times daily and continued, with due regard for disagreeable by-effects, for several weeks, if necessary. When there is much restlessness, potassium bromid or codein, in small doses, will be found a useful adjuvant. In the hands of Berkley, Dercum and others parathyroid extract in doses of $\frac{1}{20}$ to $\frac{1}{10}$ grain (0.003–0.006 gm.), three times daily, seemed to be of temporary benefit.

## TETANY

**Definition.**—Tetany is a disease characterized by intermittent tonic muscular spasms, especially in the hands and arms, and increased excitability of the peripheral nerves.

**Etiology.**—Tetany appears to be more common in Central Europe than elsewhere. In this country it is comparatively rare. It affects chiefly infants and young adults. A family predisposition has occasionally been noted. The disease occurs most frequently in the winter and spring. Infantile tetany is usually associated with rickets, gastrointestinal disorders or acute infections. Tetany of adults develops under the most diverse conditions. (1) It may occur epidemically. This form has been observed especially in Europe. It attacks chiefly healthy young workingmen and seems to show a predilection for certain trades (tailoring and shoemaking). (2) Tetany sometimes occurs in the course of gastrointestinal affections, most frequently with gastrectasis due to pyloric stenosis, but occasionally with chronic diarrhea, dilatation of the colon, mucous colitis, helminthiasis, etc. (3) It may develop in pregnancy (usually between the fifth and eighth months) or during lactation. (4) It has followed the accidental removal of excessive amounts of parathyroid tissue during thyroidectomy (tetania parathyreopriva). (5) It rarely appears in the course of infectious diseases, such as typhoid fever, measles, influenza, etc. In a few instances it has been noted as a terminal complication of tuberculosis. (6) It has been observed in various intoxications, as from chloroform, alcohol, ergot, morphin, and uremia. (7) It may result from the ingestion of large doses of sodium

[1] Boston Med. and Surg. Jour., Nov. 21, 1918.

bicarbonate (alkalosis). (8) It can be induced by forced respiration or overventilation of the lungs.

**Pathogenesis.**—The nature of tetany is obscure. The researches of Moussu, Vassale, MacCallum, Voegtlin and others indicate that the disease is due, at least in many instances, to deficient secretion in the parathyroid glands. Removal of these glands results in hyperexcitability of the nerves, tetany, and death; reimplantation of parathyroid tissue and even the administration of parathyroid extracts suppress the tetany symptoms. Apparently the parathyroid glands in some way control calcium metabolism, and various attempts have been made to bring the phenomena of tetany into causal relation with a lack of available calcium in the circulating fluids. Removal of the glands is said to be attended with a loss of calcium (MacCallum) and with interference with ossification (Erdheim); a decrease in the concentration of calcium in the blood has been observed in tetany (Howland and Marriott); and the administration of calcium salts arrests temporarily the convulsive paroxysms in affected animals. Other procedures, however, seem to be equally or more effective. Recently D. W. Wilson and his co-workers[1] have shown that parathyroidectomy is soon followed by a condition of alkalosis, which is neutralized by the acid products generated by the tetanic muscular contractions, and that the administration of acids is even more efficacious in experimental tetany than that of calcium. Wilson's observations, which have been verified by McCann,[2] harmonize with the facts that tetany may be produced by the administration of large doses of sodium bicarbonate and also by forced respiration, overventilation of the lungs tending to remove carbon dioxid from the blood (Grant and Goldman,[3] Collip and Backus[4]). The relation of parathyroid deficiency, of low calcium content of the blood, and of alkalosis to one another still remains to be determined.

**Symptoms.**—The muscular spasms occur in attacks lasting minutes or hours and recur at intervals of hours or days. They are usually preceded by general malaise and paresthesiæ (numbness, formication, burning) and are frequently painful. They are almost always bilateral and most commonly affect the hands and forearms, the hands assuming an "obstetric position," with the thumbs and fingers adducted, the proximal phalanges flexed, and the distal phalanges extended. From the hands the spasms frequently spread up the arms, causing flexion of the wrists and elbows. Not rarely the legs are also attacked, the feet being inverted and the toes flexed (talipes equino-varus), and occasionally the muscles of the trunk, neck and face become involved. Ocular spasms were observed in 7 of Frankl-Hochwart's[5] 122 cases. In children spasm of the larynx is not uncommon, and in some instances it is the dominant feature. General epileptiform convulsions sometimes occur, especially in infancy. In the absence of convulsions, consciousness is retained and the mentality is, as a rule, clear, although confusion and hallucinations may be seen (Kraepelin). Objective sensory disturbances are absent and the tendon reflexes are normal or somewhat increased.

In addition to the spasms, there are important indications of increased excitability of the peripheral nerves. These are known as the Trousseau, the Chvostek, the Erb, and the Hoffmann signs. Trousseau's sign is the occurrence during the passive intervals of typical spasms upon forcible com-

[1] Jour. Biol. Chem., 1915, xxi and xxiii.
[2] Jour. Biol. Chem., 1918, xxxv.
[3] Amer. Jour. Physiol., 1920, lii.
[4] Jour. Missouri State Med. Assoc., May, 1920.
[5] Die Tetanie der Erwachsenen, Wien, 1907, 2d edit.

pression of the principal nerve trunks of the affected limbs, more especially of the arms. It is almost pathognomonic of tetany, but it is absent in about one-fourth of the cases. Chvostek's sign is another indication of increased mechanical irritability of the nerves. It consists in the occurrence of quick muscular contractions at the ala of the nostril, at the corner of the mouth, or over the entire area innervated by the seventh nerve, when the latter is sharply tapped with the finger. Sometimes mere stroking of the cheek is sufficient to call forth the contractions (Schultze's phenomenon). Chvostek's sign has been observed in other conditions and is absent in many cases of tetany, especially in children. Erb's sign consists in greatly increased electric excitability of the nerves. Very weak galvanic currents (0.1 to 0.7 miliampère) induce cathodal closure contraction and slightly stronger currents excite cathodal closure tetany. In children the occurrence of cathodal opening contractions with currents under 5 milliampères and the occurrence of anodal opening contractions with less current than that causing anodal closing contractions is characteristic of tetany (Mann, Thiemich, Holmes).[1] Hoffmann's sign, which is less important, depends upon increased irritability of the sensory nerves. Pressure and weak galvanic currents cause paresthesia and even painful sensations.

In the more chronic cases secretory and trophic phenomena, such as hyperidrosis, puffiness of the face, cyanosis of the hands, urticaria, and alopecia, cataract, and changes in the nails, are occasionally observed. Frankl-Hochwart recognizes a latent form of the disease (*forme fruste*), in which the only manifestations are increased mechanical and electric excitability of the nerves and paresthesia.

**Course and Prognosis.**—The duration varies from a few hours to many months or even years. It is usually several weeks. Remissions mark the more protracted cases. Recurrences are not uncommon and frequently occur at regular intervals. The prognosis, on the whole, is favorable, although in tetany of gastrectasis the mortality is high (50–75 per cent.) and in the infantile form eclamptic attacks and spasm of the larynx sometimes lead to a fatal result. The mortality of tetany in pregnant women is about 7 per cent. The idiopathic type occurring in artisans rarely kills, but it is prone to become chronic or to recur at varying intervals. Parathyroprival tetany, when severe, not rarely proves fatal. In some cases it becomes chronic. Eiselberg[2] cites 2 cases which persisted for 21 and 39 years respectively.

**Diagnosis.**—This is easy in well developed cases. In *tetanus* the spasms are more continuous, the muscles of the jaw are, as a rule, first affected and then those of the neck and trunk, and a primary source of infection is usually found. In *hysteria* the muscular contractions are frequently unilateral, anesthesia and other stigmata of hysteria are present, and Trousseau's and Erb's signs are usually wanting, although they may occur as a result of suggestion.

**Treatment.**—The cause should be sought for and removed, if possible. In infants dietetic and hygienic regulations are of prime importance. When there is evidence of rickets, cod-liver oil and phosphorus are of definite value. In the form associated with gastrectasis, lavage, rectal feeding, and proctoclysis with normal saline solution are sometimes of serivce. If the condition does not improve gastroenterostomy should be performed. Wirth[3] has collected 21 cases treated surgically, with a mortality of 15 per cent., as

[1] Amer. Jour. Dis. Child., 1916, xii, 1.
[2] Arch. f. klin. Chirurg., 1921, cxviii, 387.
[3] Centralbl. f. die Grenzgebiete der Med. u. Chir., 1910, xiii, No. 21.

compared with a mortality of 50 to 75 per cent. in the cases treated by medical means. In cases occurring during lactation benefit accrues from weaning the child. In all cases rest in bed, frequent warm bathing, and restriction of the diet to light unstimulating foods are general measures of value. Lumbar puncture has proved efficacious in some instances. Calcium is indicated. It may be prescribed as calcium lactate or glycerophosphate. Parathyroid preparations have been employed with some success, but as a rule they have failed. For the spasms themselves, sedatives, such as bromids, chloral, and scopolamin, may be used.

## TIC

(Convulsive Tic; Impulsive Tic; Habit Spasm)

Tic is a psychomotor affection manifested by coördinate purposive movements, closely imitating physiologic acts, but unnatural in their involuntary reproduction, inopportuneness, intensity and frequency of repetition. It occurs in neuropathically predisposed individuals in response to some accidental cause, such as local irritation, imitation, mental shock or trauma. The original movement may have been voluntarily executed, but in the subject with a tendency to tic it is repeated even after the exciting cause has ceased to act and soon it becomes habitual and automatic.

The motor reaction of tic is often confined to a single muscle or group of muscles, but there are cases of extreme severity in which the entire body is affected (*maladie des tics* of Gilles de la Tourette). Among the most common forms of tic may be mentioned frequent blinking of the eyes (nictitation), involuntary rotation of the eyeballs, licking tic, in which the lips are repeatedly moistened by the tongue, snuffling tic, jerking of the head, and shrugging of the shoulder. Not infrequently the larynx is affected causing grunting or other inarticulate sounds, and occasionally, as in Gilles de la Tourette's disease, the movements are accompanied by an irresistible impulse to utter profane or obscene words (coprolalia). Tic of the lower extremities is comparatively rare.

The movements are always a repetition of the same act, although extensions may occur through the involvement of adjoining and functionally related muscles. They are aggravated by excitement, disappear during sleep, and can be controlled to a certain extent by the will, and not infrequently at times by slight pressure or even some trick of restraint which the patient has learned to practice. Execution of the movement affords a measure of satisfaction, whereas suppression is associated with a certain degree of tension or uneasiness. With the exception of spasmodic torticollis —the "mental torticollis" of Brissaud—which is not rarely the sequel of ordinary "stiff neck," the motor reactions of tic are usually clonic. Although subjects of tic, *tiquers*, are often highly intelligent, they usually present on careful investigation definite evidence of mental and emotional instability.

The movements of *chorea* differ from those of tic in being incoördinate, purposeless, and ever changing. The contractions of *paramyoclonus multiplex* in contrast with those of the syndrome of Gilles de la Tourette are irregular and purposeless, and usually limited to the extremities and trunk. Clonic contractions of the facial muscles occur in a number of conditions which resemble more or less closely tic. *Spasms of cortical origin* (focal epilepsy) occur in paroxysms, involve the different muscles of the face successively rather than simultaneously, and are usually attended by other

signs of epilepsy, such as pallor, unconsciousness, post-epileptic exhaustion, etc. *Spasms of peripheral origin,* excited by a lesion in the seventh nerve itself or in its nucleus, unlike the contractions of tic, are strictly limited to the area of distribution of the facial nerve, cannot be suppressed by an effort of the will, often persist during sleep, and instead of reproducing a natural purposive act conform exactly to the contractions excited by an electric current. Exceptionally, such facial spasms are accompanied by severe pain simulating trigeminal neuralgia. *Hysterical contractions* are occasionally met with, sometimes in connection with spasm of the muscles of the tongue upon the same side. The differential diagnosis depends upon the presence of other evidences of hysteria and upon the exclusion of every other form of contraction.

The prognosis of tic is doubtful. Complete cure is often effected in children but seldom in adults. Spasmodic torticollis is especially rebellious to treatment. Gilles de la Tourette's disease is progressive and incurable. The treatment of tic consists in removing any existing peripheral irritation which may have served as an exciting cause, such as errors of refraction or intranasal lesions, and in employing general measures to combat the underlying constitutional inferiority. Graduated gymnastic exercises are especially useful. Children subject to tic require careful training and protection from all influences which tend to excite the emotions. In some cases much benefit is derived from the reëducational exercises introduced by Brissaud. Briefly these are "a combination of immobilization of movements with movements of immobilization." Certain exercises are intended to teach the patient how to preserve immobility, while the object of others is to replace an unwilled movement by one that is willed. The exercises in general have to be performed in front of a mirror. The excellent monograph of Meige and Feindel[1] should be consulted in this connection.

## PARAMYOCLONUS MULTIPLEX

This rare form of myospasm, first described by Friedreich[2] in 1881, is characterized by involuntary clonic contractions of the muscles similar to those produced by an electric shock. It may be constant or paroxysmal. Any or all of the voluntary muscles may be affected, except those of the eye, but usually the muscles of the limbs, especially of the proximal portions, are chiefly involved. In most cases the contractions are confined to individual muscles and cause little or no movement of the limb in which they occur; indeed, there may be only wave-like movements through the muscle (myokymia) or merely twitching of the individual fibers (fibrillation). As a rule, the contractions are lessened by voluntary effort and cease entirely during sleep. On the other hand they are intensified by irritation of the skin or muscles, exposure to cold, and excitement. Electric contractility, sensation and intelligence remain normal. The nature of the disease is obscure. No causal lesions have been found, but the contractions appear to be irritative manifestations referable to direct or reflex excitation of the peripheral (spinal) motor neurons (Hunt).

Paramyoclonus multiplex appears to be closely related to the *electric chorea of Henoch. Dubini's electric chorea,* which seems to be confined to

[1] "Tics and Their Treatment," by Henry Meige and E. Feindel. Translated by S. A. K. Wilson, London, 1907.

[2] Virchow's Arch. f. path. Anat., 1881, lxxxvi, 421.

northern Italy, is a different affection. It is probably an infectious form of encephalomyelitis and is usually fatal. The movements are violent, are frequently preceded by pains in the head and back, are accompanied by convulsive attacks and are followed by paresis and wasting of the affected muscles. In *ordinary infectious chorea* (Sydenham's chorea) the movements are less abrupt, more changeable, more likely to involve the face, of wider range and with marked locomotor effect, in contrast to the muscle jerks and twitchings of myoclonus. The movements of *tic* differ from all other myoclonia in being purposive, coördinate and such as normal persons often execute. Paroxysms of lightning-like contractions of the muscles occur in the *myoclonus epilepsy* of Unverricht, but in this disease there are also attacks of epilepsy of the *grand mal* type and evidences of marked degeneracy are usually present. Muscle jerks or twitchings of the myoclonus or myokymia type are sometimes observed in *epidemic encephalitis*, but the occurrence of delirium and other encephalic features, the frequent involvement of the abdominal muscles in the movements, and the coexistence of more typical cases of the disease in the community will usually make the diagnosis clear. *Hysterical movements* differ from those of paramyoclonus multiplex in being, as a rule, more purposive, of large amplitude, more productive of locomotor effects, and more variable, and in being associated with other stigmata of hysteria.

The **prognosis** of paramyoclonus multiplex is uncertain, although complete recovery is not uncommon. In regard to **treatment** benefit may be derived from the application of strong galvanic currents to the spine, and the administration of tonics and such sedatives, as bromids, scopolamin, etc.

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# NEUROSES

## EPILEPSY

Convulsive seizures with loss or impairment of consciousness result from widely varying causes. After eliminating from consideration those that are due (1) to hysteria, (2) to uremia, (3) to puerperal eclampsia, (4) to certain exogenous intoxications (alcoholism, plumbism), (5) to coarse lesions of the brain (tumor, gumma, meningitis, etc.), (6) to arteriosclerosis of the cerebral vessels, (7) to serious traumatic injuries to the brain (hemorrhage, depression of bone, etc.), (8) to heart-block (Stokes-Adams syndrome), and (9) those that occur in infancy as a result of reflex irritation, as an accompaniment of tetany, as an initial symptom of some acute infectious disease, or as a concomitant of idiocy, hydrocephalus, etc., there still remain others which cannot be traced to any obvious or adequate cause, except, perhaps, an inherited neuropathic disposition, and which recur from time to time, either spontaneously or in response to some trivial irritation, through a period of many years. It is to the obscure basic condition producing convulsions of the last group that the name of "*essential*" or "*idiopathic*" *epilepsy* is commonly given. Doubtless, even so-called essential epilepsy is not a single entity, but the clinical expression of a multiplicity of cerebral changes, differing widely in their character and origin, and that as our knowledge of the subject increases the application of the term will become appreciably more restricted.

**Definition.**—Epilepsy may be defined as a chronic cerebral disorder, without obvious causal lesions, usually founded on hereditary neuropathic predispositon, and characterized by the occurrence at varying intervals of attacks of transient loss or impairment of consciousness, with or without convulsions, and by the gradual supervention in many cases of more or less pronounced mental deterioration.

**Etiology.**—An hereditary neuropathic predisposition is the most important causal factor. In a large proportion of cases a family history of epilepsy itself or of insanity, psychasthenia, migraine, hysteria, tic or chorea in the antecedents and present or past collaterals is obtainable. Alcoholism in the parents is also believed to be effective, but owing to the great prevalence of alcoholism it is difficult to determine accurately the potentiality of this factor. Traumatism is responsible for some cases; excluding those, however, in which definite anatomical injury to the skull and brain has been produced (symptomatic epilepsy) the proportion is small. The acute infectious diseases, notably scarlet fever, measles, cerebrospinal fever and pertussis, are not without influence. It may be that in epilepsy of infectious origin is in some instances symptomatic and based upon minute foci of encephalitis or sclerosis. Emotional shock (fright, profound grief, etc.) sometimes serves as an "agent provocateur" of epilepsy when the predisposition is already present. Likewise, constant peripheral irritation arising from ocular defects, nasal obstruction, painful scars, phimosis, etc., occasionally arouses a preëxisting dormant epilepsy, but undoubtedly the importance of this factor has been greatly over-estimated. It has been shown that infantile eclampsia occurring in association with acute indigestion, teething, fever, the presence of intestinal worms, etc. is most frequently observed in families with an inherited neuropathic taint, and that not rarely it is the precursor of confirmed epilepsy in later life. For these reasons it is often impossible to say where the one condition ends and the other begins. Finally, it should not be forgotten that epileptic seizures dating from early childhood may be dependent upon a meningo-encephalitis occurring at or before birth, even when the lesions of this condition are too slight to be proclaimed by other phenomena, such as imbecility and hemiplegia.

Epilepsy occurs about as frequently in one sex as in the other. In the large majority of cases it develops in the period between birth and the twentieth year. Infancy and puberty are the two epochs in which it is most likely to appear. Few cases begin after the twenty-fifth year.

When the affection already exists, individual attacks may occur spontaneously or in response to certain accidental causes, such as mental or physical overexertion, emotional disturbances, indigestion and constipation. In females the seizures are especially prone to occur during or immediately before the menstrual periods.

**Pathology and Pathogenesis.**—Up to the present time no constant pathologic lesions have been demonstrated in the brains of epileptics. Certain histologic changes in the cerebral cortex—degenerative atrophy of the nerve cells, perivascular infiltrations, punctiform hemorrhages and overgrowth of the glial tissue—have been described but in some instances, at least, these may be effects and not the cause of the paroxysms. Despite an enormous amount of clinical and experimental work the intimate nature of the disease still remains obscure. Some contend that the attacks arise autochthonously owing to an inherent anomaly of the cortical centers; others ascribe them to autointoxication, others to reflex irritations, and others, again, to cerebral anemia induced by vaso-constriction and cardiac inhibition.

**Symptoms.**—The *Major* or *Complete Attack* (*Grand Mal*).—In about one-third of all cases the epileptic attack is preceded by certain premonitory

symptoms. These sometimes extend over several hours or days (remote prodromes) and consist of chilliness, indigestion, lassitude, irritability of temper, mental depression, or, more rarely, of a feeling of extraordinary exhileration and buoyancy. As a rule, however, the premonitions last a few seconds only and really constitute the iniatory symptoms of complete seizures. Since the time of Galen these immediate prodromes have been known as *auræ*. Most frequently, perhaps, the patient experiences some peculiar sensation, which arising from the epigastrium, the precordium, an arm, a leg, or some other part, seems gradually to ascend until it reaches the neck or head, when unconsciousness suddenly supervenes. Not rarely the warning comes through one of the special senses, especially sight or hearing. Ocular auræ may consist of double vision, sudden blindness, flashes of light, vivid "stars," or actual hallucinations of sight—faces, figures, or scenes. In auditory auræ various subjective noises or even definite words may be heard. Auræ of taste and smell also occur, but are rare. Sometimes the approach of a seizure is heralded by vertigo, nausea and vomiting, or palpitation. In other cases the attack is ushered in with transient psychic disorders. These may take the form of mental confusion, vague sensations of fear or anguish, "dreamy states," sudden impulses, automatic actions, aphasic speech disturbances, or, more rarely, maniacal outbreaks. Occasionally the aura is motor and consists of clonic contractions or a tonic spasm of certain muscles. Whatever its character, the aura does not usually change in succeeding attacks in the same patient.

After the aura, or without any warning, the patient suddenly loses consciousness, and, if standing falls heavily to the floor, sometimes severely injuring himself. In many cases just before the fall there is a shrill scream or a low groan, which is to be ascribed to spasmodic contraction of the respiratory muscles. With the occurrence of insensibility the patient's face becomes intensely pale and his whole body rapidly passes into a state of rigidity or tonic spasm, in which the distortions are usually as follows: The head is retracted and strongly inclined to one side, the teeth are firmly set, the forearms are flexed, the fingers clinched over the thumbs, and the legs and feet extended. The eyelids are open, the eye-balls are turned upward and to the same side as the head, and the pupils are dilated and immobile. In consequence of the arrest of respiration and compression of the veins intense congestion and lividity soon replace the pallor and not rarely slight hemorrhages occur into the conjunctiva or skin. In from 10 to 30 seconds jerky vibratory movements begin in the face and limbs and rapidly develop into violent clonic contractions. The pupils oscillate, the eye-balls twitch, the teeth are ground together exposing the tongue to injury, frothy saliva, often blood-streaked, appears at the mouth, the arms and legs are alternately flexed and extended, and not infrequently the urine and feces are expelled. In the course of two or three minutes the convulsive movements subside, the patient draws a deep sigh, the muscles relax, and the cyanosis disappears. Consciousness may return at once but in the majority of cases the coma is succeeded by profound sleep, which sometimes lasts several hours. On waking, the patient suffers from mental confusion, headache, general muscular soreness, languor, and occasionally from nausea and vomiting. More rarely, the paroxysm is immediately followed by temporary mental derangement, which may take the form of intense emotional excitement with hallucinations of sight or hearing, of maniacal delirium, perhaps impulsive and dangerous, or of automatism, a condition in which certain purposive acts are performed wholly unconsciously. Occasionally after severe attacks transient paresis of one limb or of one side of the body (exhaustion paralysis) is observed.

Temporary aphasia, deafness, or amblyopia may also occur. Sometimes there is a slight elevation of temperature and not rarely the urine contains a trace of albumin and a few hyaline casts. The reflexes are variable. In many cases, however, even within an hour after the attack the knee-jerks are exaggerated and Babinski's sign is present on one or both sides.

*Other Forms of Attack.*—In many cases the fit does not advance beyond the iniatory symptoms of the major attack. Sometimes there is only a momentary loss of consciousness, without an aura or any indication of motor spasm. In such seizures the patient may abruptly stop in the midst of his work or conversation, stare vacantly into space for a few seconds, and then immediately go on with what he was doing, perhaps entirely unconscious of the interruption; or during the brief insensibility the patient may turn pale, catch his breath, stagger, let drop anything he may be holding in his hand, or involuntarily void urine. In other cases there is only obscuration of consciousness and the seizure is represented chiefly by vertigo, a dreamy, "twilight" state (Dämmerzustände), a sudden sensation of fear or horror, an hallucination of the special senses, or, rarely, by cardiac palpitation or an outbreak of sweat. Occasionally, the seizure is reduced to isolated clonic contractions or a sudden jerk of the limbs, consciousness being neither lost nor impaired. To all these slight or rudimentary attacks the term *minor epilepsy* or *petit mal* is applied. Between the minor and major forms every graduation of paroxysm is observed. *Petit mal* occurs, as a rule, in the intervals of complete seizures, but it may be the sole expression of the disease.

*Partial or Jacksonian Epilepsy.*—In some instances the convulsive movement is limited to one part as the face, or begins in one member and then radiates to a variable extent, ultimately involving, perhaps, a lateral half of the body. Consciousness may or may not be retained. This type of spasm is known as Jacksonian epilepsy, after Hughlings Jackson, who first described it in 1861. It is by no means uncommon in essential epilepsy, athough it often signifies focal disease of the motor cortex and occasionally it is traceable to a tumor in a part of the brain remote from the cortex, to an old injury of one of the extremities (reflex epilepsy) to an intoxication or even to hysteria.[1]

*Procursive epilepsy* (*epilepsia procursiva*) is a form in which the patient automatically performs movements of walking or running and then regains normal consciousness or falls in a convulsive seizure. As a rule, no aura precedes the automatic propulsion, but not rarely there is a shrill cry or a rapid repetition of certain words or phrases.

*The Status Epilepticus* is an acute manifestation of epilepsy in which convulsions follow one another in rapid succession over a period of many hours, unconsciousness being continuous between the seizures. The condition is nearly always accompanied by a marked rise of temperature, increased frequency of the pulse and respiration, and great exhaustion. A fatal termination often follows. According to Clark and Prout[2] in about one-third of the status cases the seizures are dependent upon organic lesions of the cerebral cortex acquired in early infancy.

*Psychic Epileptic Equivalents and Psychic Epilepsy.*—It is now generally recognized that mental disturbances may occur not only immediately before or after epileptic seizures, but that in certain cases they may actually replace from time to time ordinary attacks of *grand mal* or *petit mal*, and

[1] See article by George Wilson, Jour. Amer. Med. Assoc., Mar. 26, 1921.
[2] Amer. Jour. of Insanity, Oct., 1893.

form what are known as psychic epileptic equivalents, and, further, that temporary mental derangements, involving an obscuration of consciousness, may rarely occur entirely independently of other epileptic associations and constitute what has been described as pure psychic epilepsy—*épilepsie larvée pure* of the French writers. In individual cases the epileptic equivalents usually coincide with the mental states that occur in conjunction with convulsions. The duration of such attacks varies from a few minutes to several days, and, as a rule, both onset and termination are sudden. In psychic epilepsy the paroxysms are likely to assume the form of automatic actions, the patient going about for hours and even for days performing ordinary acts, as if he were still in his usual senses, but having no recollection whatever of his performances after consciousness returns.

*Myoclonus epilepsy* is the name applied to a rare affection, first described by Unverricht in 1891, in which myoclonia and epilepsy are combined. In the intervals of major epileptic seizures there are paroxysmal clonic contractions of the muscles of the extremities, especially of the proximal portions, and more or less persistent fibrillary tremors. The disease is usually found in several members of the same family. It resembles somewhat the equally rare disorder designated by Koshewnikow[1] as *partial constant epilepsy* (*epilepsia partialis continua*), but in this the interparoxysmal tic-like twitchings are limited to a small portion of the body.

The **frequency** of epileptic attacks varies considerably according to the severity of the disease, the general health of the subject and the external influences by which he is surrounded. Seizures may occur as seldom as once in two or three years or as often as 15 or 20 times a day. A striking regularity in the periodicity of attacks is often observed, and in some cases, especially of *grand mal*, the attacks tend to occur in groups or series with comparatively long intervals of freedom. In women such cumulative outbreaks often take place at the menstrual periods. In some epileptics the fits appear exclusively at night, during sleep (*nocturnal epilepsy*). This type may readily escape recognition. It is to be suspected when nocturnal enuresis develops in late childhood, or when the patient complains of waking from time to time languid and bruised, or with ecchymoses in his skin, or with his tongue sore. Intercurrent diseases, notably the acute infections, not rarely exert a marked inhibitory influence on the seizures of epilepsy. Pregnancy may either increase or diminish the frequency of the paroxysms. It is noteworthy also, as Féré[2] first pointed out, that puerperal eclampsia sometimes marks the onset of confirmed epilepsy in predisposed persons.

In the *intervals* between attacks many epileptics appear to enjoy good health, both mental and physical. As a rule, however, they are inclined to be irritable, supersensitive, self-conscious, self-important, impulsive, and obstinate. Not a few of them exhibit also structural stigmata of degeneration, such as asymmetry of the face or cranium, abnormal implantation of the teeth, a high arched palate, anomalies of the external ears, etc. In a large proportion of cases, although by no means in all, after the disease has lasted some years, particularly if it has begun in early childhood, if the fits occur at frequent intervals, and if *grand mal* and *petit mal* coexist, a gradual weakening of the intellectual capacity takes place and ultimately the patient becomes more or less demented.

[1] Neurol. Centralbl., 1895.
[2] Féré, Les épilepsies et les épileptiques, Paris, 1890.

**Diagnosis.**—Most cases of epilepsy are recognized without difficulty, but certain incomplete forms may readily lead to error. Neither the patient nor the patient's friends in many instances have any idea of the connection between slight attacks, or the phenomena that they allude to as "weak spells," "faint" or "lapses," and the seizures of major epilepsy; hence all attacks of unconsciousness or vertigo that come on abruptly, last a brief time, terminate suddenly, and occur periodically apart from other associations should be investigated with great care. In ordinary *syncope* unconsciousness usually occurs less abruptly and after effects, such as malaise and mental confusion are less common. *Labyrinthine vertigo* resembles *petit mal* in being definitely paroxysmal, but as tinnitus and deafness are always present in the intervallary periods of the former confusion is not likely to occur. Convulsions occurring as intercurrent phenomena in *cerebral tumor and other gross lesions of the brain* may usually be distinguished by the previous history and the other characteristic symptoms of these affections, such as persistent headache, vomiting, choked disc, and focal paralysis. Epileptic attacks of the Jacksonian type are always suggestive of an organic foundation, but are by no means pathognomonic. The syncopal or epileptiform attacks occasionally observed in *hypopituitarism* may be differentiated by the concomitant symptoms of endocrine disturbances. (See p. 867.) Cases of *paretic dementia* with epileptiform seizures as a prominent feature are usually made clear by the interparoxysmal symptoms, which include a change in the disposition and character of the patient, quivering of the muscles about the mouth, pupillary anomalies, a halting tremulous speech, a vacant mask-like expression, delusions of grandeur and general muscular weakness. Moreover, in paretic dementia evidence of syphilis is almost invariably obtainable and the cerebrospinal fluid shows definite alterations. Convulsions due to *lead poisoning*, *alcoholism*, and *uremia* are almost always sufficiently explained by coexisting signs and symptoms.

The state of abnormal irritability in infants to which Thiemich[1] gave the name *spasmophilia* may readily be confused with epilepsy, especially if general convulsions are among its manifestations. Spasmophilia occurs chiefly in bottle-fed infants, and is commonly associated with rickets. It is more closely related to tetany than to epilepsy, and may usually be recognized by the tendency to local spasms, such as holding the breath, laryngospasm and tonic contractions of the hands and feet; by the occurrence of multiple attacks in rapid succession; and, above all, by the increased mechanical excitability of the nerves and altered electrical reactions, which are described in the discussion of Tetany (see p. 1022). However, spasmophilia may coexist with epilepsy and doubtless some spasmophilics are potential epileptics.

The differentiation of *hysteria* from essential epilepsy is not always easy. Attention to the following points, however, will usually lead to a correct diagnosis. In hysteria the attacks are often directly traceable to psychic excitement, appear less suddenly, last longer, and do not end in deep sleep or coma; the body is not often injured in the fall, nor is the tongue bitten; urine is not voided involuntarily; consciousness is seldom completely lost and emotional displays are common; the pupillary reflexes are almost always intact; the tetanic spasm affects chiefly the muscles of the neck and back; the clonic contractions often bear the character of voluntary movements;

[1] Münch. med. Woch., 1899, xlvi, 1449.

and finally there is no tendency to dementia, the permanent mental condition of the hysteric being entirely different from that of the epileptic.

**Prognosis.**—Epilepsy does not necessarily shorten life, although it increases somewhat the risks to life. Aside from the *status epilepticus*, which often ends fatally, individual seizures are not usually dangerous. Death may occur, however, from a fall, asphyxia or cerebral hemorrhage. The semi-invalid life that many epileptics are compelled to lead also favors the occurrence of certain other diseases, notably tuberculosis. Complete recovery in essential epilepsy is unusual. The proportion of cases in which it occurs probably does not exceed five per cent. However, under persistent, judicious treatment great amelioration may be achieved in many cases, and not rarely there are spontaneous remissions, sometimes lasting for several years. In general, those cases may be regarded as the most favorable, so far as the likelihood of improvement and escape from mental degradation are concerned, in which the onset is after the tenth year, in which structural stigmata of degeneration are absent, in which the seizures conform to the major type and occur at long intervals, and in which the duration of the malady is less than four or five years. On the whole *petit mal* is less tractable than *grand mal*. In pure psychic epilepsy the outlook is grave. The comparatively rare form of the disease which develops after 30 years of age offers a comparatively favorable prognosis, provided, of course, the attacks are not symptomatic of some organic cerebral lesion or of alcoholism.

**Treatment.**—Hygienic treatment is of the utmost importance. Moderate exercise, both mental and physical, is beneficial. Idleness and seclusion have a baneful effect. Adults should follow, if possible, some light and agreeable pursuit, frequently one which will permit them to spend the greater part of the day in the open air, and which will not add to the risk of physical injury should attacks come on without warning. The establishment of so-called epileptic colonies or farms, where patients can be employed in agricultural pursuits, has proved a great boon to many comfirmed epileptics of the bread-winning class. Children in whom the disease is well established are better cared for, as a rule, in special institutions or private sanitoria. Home training to be successful usually requires the services of a capable supervisor. The marriage of epileptics should be discouraged.

The diet should be simple, readily digestible, and, in most cases, mainly vegetable. Overloading of the stomach is a potent factor in precipitating attacks. The principal meal is best taken at midday, and full evening meals should be avoided. The claim made by Toulouse and Richet[1] that it is advantageous to reduce the sodium chlorid taken with food to one or two grams a day has been confirmed by many observers.

Tea, coffee, alcohol, and tobacco should be used very sparingly, if at all. The patient must be constantly warned against excesses of every kind. The digestive functions should be brought to the highest possible state of efficiency. The bowels must be regulated by diet, and, if necessary, by mild aperients. Liberal water-drinking, frequent bathing, followed by friction of the skin, light exercise in the open air, and other measures which favor elimination are to be recommended. General tonics, such as iron, arsenic, and cod-liver oil, are sometimes required to combat anemia and malnutrition.

Although very few cases of epilepsy are purely reflex, peripheral irritation—phimosis, adherent prepuce, worms, a foreign body in the nose or ear, and painful cicatrices—should be carefully sought for, and if found removed.

[1] Acad. des Sciences, 1899, 20, xi.

The most reliable drugs are the bromids. The amount required varies with the severity of the case and the susceptibility of the individual, and must be determined experimentally in each case. A daily dose of from 1 to 1½ drams (4.0–6.0 gms.) of sodium or potassium bromid should not be exceeded. The addition of one or two drops of Fowler's solution with each dose of bromid is useful in preventing the occurrence of acne. When the attacks occur at regular intervals it is advisable to administer the drug in relation to the time of the attacks. Thus, in nocturnal epilepsy a single large dose at bedtime may suffice. Again, in women, when the seizures occur only at the menstrual periods, active medication may be restricted to the week preceding each period. When the convulsions occur at long intervals and show no tendency to increase in frequency, its better to dispense with special medication entirely and to rely upon hygienic and dietetic measures to lessen the excitability of the nerve-centers. In every case it is of the utmost importance to limit the dose of the bromids to the smallest possible amount that will control the seizures. Relief that comes only with saturation is dearly purchased.

Luminal, which is veronal with an ethyl group replaced by one of phenyl, is sometimes a very good substitute for the bromids. In doses of from ½ to 2 grains (0.03–0.13 gm.), two or three times a day, it can often be taken for long periods without untoward effects. Psychic depression and apathy, however, may occur, and occasionally the drug seems actually to increase the tendency to seizures. In nocturnal epilepsy chlorbutanol (chloretone), in doses of 5 grains (0.3 gm.) is sometimes a useful adjuvant to the bromids. Horse-nettle is another remedy that may increase the efficacy of the bromids. From ½ to 1 dram (2.0–4.0 mils) of the fluidextract may be given thrice daily. Turner[1] speaks favorably of Gélineau's dragées (six a day), which contain potassium bromid, 1 gram; picrotoxin, ⅓ mg.; and antimony arsenate, ½ mg., and Dercum[2] has found small doses of thryoid extract useful in some cases. When the circulation is weak a combination of digitalis with the bromids sometimes proves efficacious.

*Surgical Treatment.*—Trephining offers some hope of relief in certain cases of epilepsy, although it has to its credit less than 4 per cent. of recoveries. It is definitely indicated in traumatic cases if there is evidence of cranial injury and the traumatism stands in direct causal relation to the attacks. It is also indicated in Jacksonian epilepsy if there is any evidence other than the fits of a coarse cortical lesion. According to Matthiae[3] of 326 cases of traumatic epilepsy (60 of the general and 266 of the Jacksonian type) treated surgically, cure or recovery lasting several years occurred in 96, of which 81 were of the Jacksonian type.

*Treatment of the Attack.*—When an aura is perceived it is often possible to arrest the paroxysm by the inhalation of amyl nitrite. Patients may provide themselves with this drug in the form of pearls which may be crushed in the handkerchief. When the attack is preceded by a local spasm forcible extension of the part sometimes succeeds in aborting it. If a sensory aura is felt in a limb the part may be firmly grasped or encircled with a tight ligature. The patient himself often learns by experience some method by which he can suppress seizures of which there is due warning. During the attack there is little to be done beyond protecting the patient from injuring himself. If necessary inhalations of amyl nitrite or of chloroform may be used. In the status epilepticus the most reliable measures are inhalations of

[1] W. A. Turner, Morison Lectures on Epilepsy, Brit. Med. Jour., 1910.
[2] Da Costa's Hand-book of Medical Treatment, 1918, vol. i, 622.
[3] Deut. Zeitsch. f. Chir., 1913, cxxiii, 417.

chloroform, hypodermic injections of scopolamin (1/100 grain—0.00065 gm.) or of morphin (1/4 grain—0.016 gm.), enemas of chloral (20–30 grains—1.3–2.0 gm.) and hot baths.

## NEURASTHENIA

**Definition.**—Neurasthenia is a neurosis affecting various organs and functions and characterized by ready and persistent exhaustibility and increased nervous irritability.

**Etiology.**—*Secondary neurasthenia* is common. It is symptomatic of many diverse organic diseases, such as tuberculosis, syphilis, general arteriosclerosis, etc. *Primary neurasthenia* is relatively uncommon, and with advancing knowledge the number of cases ascribed to it is decreasing. Such a disease, however, undoubtedly exists. It usually shows itself first in youth or early adult life and it occurs more frequently in women than men. Neurasthenia appearing for the first time after middle age is almost always secondary to organic disease. The primary form may be acquired as a result of mental or physical overwork, intense emotional strain, the shock of an accident (traumatic neurasthenia), sexual or alcoholic excess, or an exhausting illness, but in the large majority of cases these factors merely educe a manifest disease from a latent predisposition, which is dependent upon a congenital and inherited neuropathic taint. Primary neurasthenia may, of course, coexist with organic disease without being in any way related to it.

**Pathogenesis.**—Neurasthenia is not associated with any recognizable lesions and the nature of the underlying process is unknown. It is possible, indeed probable, that some disturbance of the ductless glands is often a basic factor, but our knowledge of the subject of endocrinology is still too imperfect to reveal the exact nature of the disturbance. Some cases are best explained on the basis of Gowers' hypothesis of abiotrophy, according to which the cells possess from birth a lower vitality than normal and in consequence become exhausted or undergo atrophy early in life.

**Symptoms.**—These may be classified as motor, sensory, psychic and somatic.

*Motor Disturbances.*—Muscular fatigue after slight effort is the most constant symptom. In mild cases the sense of weakness and of weariness disappears sooner or later after cessation of effort, but in the more severe forms of the disease the recuperative power is so impaired that the patient is always tired. Although muscular insufficiency may be very pronounced, there is never any paralysis. As a result of an impaired inhibition, the tendon-reflexes, especially the knee-jerks, are usually exaggerated. A fine tremor resembling that of hyperthyroidism is often present.

*Sensory Disturbances.*—Headache is rarely absent. It may involve the brow or be diffused over the entire cranium, but in the majority of cases it is occipital and extends to the nape of the neck. Not infrequently it is accompanied by a sense of constriction about the head or a mild form of vertigo. Backache is also usually present. As a rule, it is referred to the lumbar and sacral regions, and is of a dull, dragging character. Like the headache, it is intensified by exertion or excitement. In addition to the pain, there is often pronounced sensitiveness of the entire spine or of certain vertebræ, not only to deep pressure, but to light touch. In many cases neuralgic pains, vague feelings of discomfort, and paresthesias of various kinds occur in other parts of the body, but anesthesia is never observed. Frequently,

the eyes are readily fatigued and reading soon leads to blurring of vision and headache. Disturbances of hearing are less common, but there is sometimes complaint of tinnitus.

*Psychic Disturbances.*—The most characteristic psychic phenomena are diminished capacity for continued mental work, inability to concentrate the attention for any length of time on subjects requiring much thought, and irritability of temper. Associated with these defects there are likely to be emotional depression, feebleness of volition, and a lack of self confidence and decision. Many neurasthenics become introspective, morbidly sensitive, and vaguely apprehensive. However, except in patients showing marked constitutional inferiority, the quality of the mind is not impaired; indeed it may be unusually good. Actual delusions or hallucinations are never observed. Insomnia is the rule in neurasthenia, the patient having difficulty in falling asleep or waking at frequent intervals during the night, and in the morning being weary and unrefreshed.

*Somatic Disturbances.*—Symptoms indicative of weakness and irritability of the digestive organs are present in the large majority of cases. The commonest of these are impairment or capriciousness of appetite, a sense of weight or discomfort in the epigastrium after eating, flatulence, noisy eructations, borborygmi, and heartburn. Analysis of the gastric contents rarely reveals any decided abnormality, but physical examination of the abdomen may disclose a greater or less degree of splanchnoptosis, which should be regarded rather as an evidence of general poor development than as a cause of the neurasthenia. The action of the bowels is irregular; constipation, however, is the rule. In certain aggravated cases there are attacks of mucous colitis, marked by colicky pains and the passage of large amounts of mucus or even of intestinal casts.

In many neurasthenics the heart is abnormally irritable, as shown by attacks of palpitation, by undue acceleration of the pulse upon physical or mental exertion, and occasionally by paroxysms of functional angina pectoris. Still more frequently patients present symptoms referable to vasomotor instability, such as flushing of the face upon slight excitement, flashes of heat, profuse sweating, blueness and coldness of the extremities, and excessive throbbing of the larger arteries, particularly of the abdominal aorta.

Derangements of the sexual functions often exist and not rarely dominate the clinical picture. Thus, there may be imperfect erection, premature ejaculation, nocturnal emissions, and a feeling of extreme exhaustion after coitus; or, if the case be a severe one, both sexual desire and power may be entirely lost. Such disturbances naturally react upon the patient's mind and cause great anxiety and depression of spirits. Women are more likely to suffer from hyperesthesia of the pelvic organs and dysmenorrhea than of abnormalities of the sexual functions, although symptoms of irritable weakness similar to those observed in men sometimes make their appearance.

The urinary symptoms are closely related to the digestive and circulatory disturbances and are therefore of minor importance. In many cases the urine shows an excess of urates, phosphates or oxalates, and not rarely oliguria and polyuria alternate.

**Diagnosis.**—Owing to the great similarity of the symptoms of primary neurasthenia and those of the secondary form occurring in the course of other diseases or in the prodromal stages of certain psychoses, especially dementia præcox and melancholia, it is essential to make the diagnosis by exclusion. Neurasthenic symptoms are marked in many cases of incipient tuberculosis, arteriosclerosis, arterial hypertension, chronic nephritis, hyperthyroidism, chronic prostatitis or vesiculitis, diabetes mellitus, chlorosis, drug

addiction, cerebrospinal syphilis, multiple sclerosis and paretic dementia; hence the necessity of analyzing carefully the patient's history and of making a thorough examination of the various organs, of the gastric contents, of the urine, of the blood, of the cerebrospinal fluid, and of the fundus oculi, if errors in diagnosis are to be avoided. Especially important is it to bear in mind that primary neurasthenia almost never shows itself for the first time after middle age.

Neurasthenia is sometimes mistaken for hysteria, psychasthenia, hypochrondriasis and melancholia. The points of differentiation from *hysteria* are considered on page 1043.

*Psychasthenia* and neurasthenia frequently overlap one another, but in pure psychasthenia there is no ready exhaustion and the mental condition is characteristic, its chief manifestations being timidity, lack of decision, apprehensiveness, extreme weakness of will (abulia) and a sense of utter insufficiency. Not rarely instead of vague apprehensions there are definite obsessions or actual phobias (see p. 1037). In *hypochondriasis* there are no fatigue symptoms, the essential feature being a dominating, but unfounded, conviction of illness.

*Melancholia* is a pure mental disease, the essential feature of which is profound, causeless emotional depression, with an overwhelming sense of self accusation. Fatigue symptoms are absent or are late in appearing.

**Prognosis.**—The prognosis cannot be stated in general terms. It varies considerably with the degree of constitutional or inherited feebleness, the duration and severity of the symptoms, and the circumstances and surroundings of the patient. Under favorable conditions the likelihood of clinical recovery is good, but it must be borne in mind that the process of restoration is almost always slow and tedious and that relapses and recurrences are frequent. Traumatic cases are, as a rule, especially refractory.

**Treatment.**—The treatment of neurasthenia must vary with the cause of the disease and the circumstances and idiosyncrasies of the patient. In every case an earnest effort should be made to determine the exciting cause and to remove it, if possible. With this in mind the family history of the patient, his occupation, habits, and amusements, and the condition of his various organs must be carefully studied.

In the milder forms of the disease, especially when overwork has been the exciting factor, a month or two of rest with change of scene will often effect a cure. In such cases quiet travel, so planned that it will interest the patient without fatiguing him, is frequently attended with excellent results. A prolonged sea-voyage is sometimes very useful. In other cases the "wilderness cure" of S. Weir Mitchell may be recommended with advantage.

In the absence of any special gastric disturbance, the diet should be simple, readily digestible, and abundant. Tea, coffee, alcohol, and tobacco are better avoided. A tepid sponge bath in the morning, provided it be followed by a good reaction, is beneficial. The wet pack, sitz-bath, spinal douche, and Scottish douche are of service in individual cases.

When the fatigue symptoms are marked, *rest* is imperative. This may be relative or absolute. In some cases the addition of from three to five hours to the time usually spent in bed, or a rest in bed of a few hours during the day will suffice. When, however, the symptoms are severe it will be necessary for the patient to give up all work for a period of from 4 to 8 weeks. In such cases good accrues from the "rest cure" introduced by S. Weir Mitchell. This treatment includes not only rest but also isolation, a liberal diet of easily digested foods, and artificial muscular exercise. The details must vary, of course, in each case, and only the outlines can be given here. The

full rest treatment is especially applicable to neurasthenic women; indeed men, unless they are extremely prostrated, cannot often tolerate it.

*Rest.*—For the first two or three weeks at least rest must be absolute, the patient not being allowed to feed himself nor to leave the bed to pass urine or to empty the bowels. As to this point Mitchell says: "In some instances I have not permitted the patient to turn over in bed without aid, and this I have done because sometimes I think no motion desirable and because sometimes the moral influence of repose is of use." As improvement becomes manifest some relaxation is permissible, and the patient may be allowed to sit up in bed to take meals and to indulge for a short time each day in reading or simple games. After four or five weeks he may be permitted to sit up in a chair for five or ten minutes a day, the time being gradually lengthened until at the end of a week or ten days he is up for from three to four hours. Active exercise is now cautiously introduced, and soon he is allowed to go out for a short walk or a drive. Finally, it is desirable that he should spend a week or two at the seashore or in the country before returning to his home.

*Isolation.*—This is an essential element in the treatment. No one should be permitted to see the patient except the medical attendant and the nurse. Even the writing and receiving of letters are to be forbidden. The permanent return of the patient at the close of the treatment to his family and friends should be effected very gradually. Any infringement of these rules is almost sure to mar the success of the treatment.

*Feeding.*—In most cases the diet at first should be restricted to milk. From 4 to 5 ounces should be given every two hours, and this amount gradually increased until at the end of a week or ten days from 8 to 10 ounces are given every two hours. Little by little solid food may now be added until at the end of two or three weeks the patient is getting each day three full meals with from 3 to 4 pints of milk in the intervals. The solid food may include stale bread with butter, soft-boiled or poached eggs, thoroughly cooked cereals, oysters, sweet-breads, boiled or roasted meats, green vegetables, cooked fruits, milk-puddings, and ice cream. The evening meal should be light.

*Artificial Exercise.*—This is supplied in the form of massage and electricity. Through these measures the good effects of active exercise can be secured in a measure without the expenditure of any energy on the part of the patient. Massage should not be practised until the second or third day of the treatment, and even then it should be introduced very gradually. At first the séances should not last longer than a few minutes, but ultimately they may be increased to an hour a day. It is very important, as Dercum has urged, that the massage be performed by the nurse instead of another person with whom the patient would have to become acquainted.

Electricity is the least necessary part of the treatment. It is, however, a useful adjuvant. Like the massage it should be introduced very gradually, otherwise it is likely to excite the patient and so prove harmful. A slowly interrupted faradic current is generally preferred. This should be applied once a day to each group of muscles in such strength as to elicit slight contractions.

Success in the rest treatment will depend quite as much upon the way in which the various measures are applied as upon the measures themselves. The fact must not be lost sight of that suggestion and discipline play a conspicuous part in the treatment; hence the importance of having all the details systematically and strictly carried out. It is always advisable to furnish a program indicating exactly what shall be done at each hour of the day. It

is absolutely necessary that the nurse chosen to conduct the treatment shall be not only skillful and robust but also discrete, tactful, and agreeable to the patient. Finally, the more thoroughly the physician is able to inspire confidence in the patient and to convince him that his disease is not an incurable one, the more likely is he to effect a cure.

Drugs are of little value except in meeting underlying conditions and in combating special symptoms. When there is anemia, iron and arsenic will be found useful. Small doses of strychnin are sometimes beneficial, but more often the drug is useless or actually harmful. Indigestion may be sufficiently severe to demand a modification of the dietetic treatment and the use of special remedies. Such drugs as asafetida, valerian, and sumbul are occasionally helpful.

Every effort should be made to secure sleep by general measures—tepid baths, wet-packs, and gentle massage—before resorting to drugs. If a somnifacient becomes absolutely necessary, a bromid, veronal, chloralamid or trional may be given. Chloral and morphin should be withheld on account of the grave danger of inducing a drug habit. Severe headache may call for an occasional dose of acetphenetidin or of a bromid. Constipation can usually be controlled by diet and abdominal massage, but in some cases mild, laxatives, such as cascara sagrada, sodium phosphate, or the combination of aloin, belladonna, and strychnin, will be required.

## PSYCHASTHENIA

Psychasthenia is a pure mental disease and is almost always hereditary and based upon a psychopathic disposition. It is frequently associated with neurasthenia, but it also occurs as an independent condition. Its chief manifestations are timidity, indecision, morbid doubts and scruples, apprehensiveness, a sense of powerlessness, extreme weakness of volition and obsessions of various kinds. The apprehensiveness may be vague and indefinite, but sometimes it takes the form of special fears or phobias. The latter may be of places, objects, movements or ideas. Thus, one patient may fear being alone (monophobia), another may have a fear of closed places (claustrophobia), and a third may have a fear of vehicles (amaxophobia). Not rarely the lack of inhibition results also in motor tics (*tic convulsif*) and in morbid impulses. The latter merely give rise to bizarre gestures, useless retracing of steps, frequent repetition of words in reading, utterance of oaths and expletives, etc., and never culminate in criminal acts. Some degree of emotional depression is almost always present, but throughout the patient is fully cognizant of his mental perturbations and the unreasonable nature of his acts. In pure psychasthenia the actual delusions of insanity, the stigmata of hysteria and the ready physical fatigue of neurasthenia are all wanting.

Treatment is difficult and in confirmed cases usually unsatisfactory. Good results are sometimes achieved through psychotherapy and re-education. In the absence of any mixture of neurasthenia the rest cure is rarely suitable.

## HYSTERIA

**Definition.**—Hysteria is a psychoneurosis characterized by exaggerated impressionability of the mind to suggestions from without and within and

manifested by a great variety of abnormal reactions involving the emotions, sensation, motility, and other functions under the influence of the nervous system.

**Etiology.**—Heredity is the most important of the predisposing factors. It may be direct from parent to child, but more frequently it is indirect, a neuropathic constitution being transmitted rather than the disease itself. Next in importance to heredity are faulty home training and education, and constant association with hysterical or highly emotional persons. Intense emotional disturbances, such as fright, anxiety, grief, disappointment, etc., are probably not capable in themselves of causing hysteria, but they often bring out the manifestations in persons who have a latent predisposition to the disease. Traumata of various kinds may also act as *agents provocateurs*, especially if accompanied by fright, psychic shock being the determining factor in such cases rather than the physical injury, which, indeed, may be entirely lacking. Conditions which tend to exhaust the nervous system, such as overwork, dissipation, sexual excesses, long-continued pain, and acute infection, are particularly prone to transform an hysterical predisposition into a manifest disease. Reflex influences arising from local lesions do not play any considerable etiologic rôle; nevertheless, hysteria frequently occurs as a complication of organic disease.

Hysteria is essentially a disease of young persons, and always begins in childhood or early adult life. Its manifestation may appear at any age, but never for the first time in middle life or later. Females are more frequently hysteric than males although the disparity in the two sexes is much less pronounced than many authors have stated. Race is not without influence, the disease being more prevalent and more severe among the Latin people than the Teutonic. Jews seem to be especially prone to it.

**Pathology and Pathogenesis.**—Although it is a distinct morbid entity, hysteria is not associated with any demonstrable changes in the nervous system. Indeed, as regards its essential nature nothing certain has yet been discovered. However, the extreme impressionability and emotional instability of the patient, as well as the mode of occurrence of the important sensory and motor phenomena of the disease, leave little room for doubt that the disturbance, whatever its character, is one of psychic origin. Babinski drew attention to the importance of suggestion as the exciting cause of hysteric symptoms, but as yet no adequate explanation has been offered for the patient's pathologic susceptibility to suggestion. Freud[1] believes that at the bottom of every neurosis is some interference with the normal sexual life of the patient and that the psychoneurotic symptoms depend upon a repression (Verdrängung) of disguised (unconscious) reminiscences, which are inadmissible because of their imcompatibility with prevailing moral and social standards. According to this conception hysteric phenomena are but "conversions" of the libido into other somatic manifestations. The riddle, however, remains unsolved, for even Freud postulates an innate peculiarity in the psychosexual constitution to account for the fact that some persons do not develop a neurosis under the same circumstances which prove effective in others. Freud's theory marks the third definite attempt to associate hysteria with disturbances of the sexual functions. The Greeks believed that the disease was due to migrations of the uterus to various parts of the body in search of sexual satisfaction, and even within the memory of physicians still living hysteric symptoms were commonly regarded as reflex phenomena resulting from a diseased state of the uterus or its adnexa.

**Symptoms.**—The symptoms of hysteria may be divided into the following groups: sensory, motor, mental, visceral, vasomotor and trophic.

[1] Selected Papers on Hysteria and other Psychoneuroses, Sigmund Freud, 1909.

*Sensory Disturbances.—Anesthesia* is probably the most constant of the so-called hysteric stigmata. It may involve any one or all of the varieties of sensation—touch, pain, and temperature. That of pain is oftenest affected. The loss of sensation may be absolute or partial (hypesthesia). It may extend over an entire half of the body (hemianesthesia); it may occur in small, widely disseminated areas; or, which is more frequent and characteristic, it may be limited to geometric segments of the limbs, covering them like a stocking or glove. In many cases it is confined to the skin, but not rarely it extends to the deeper tissues, notably the nerve-trunks and muscles. The mucous membranes, especially of the eyes, nose and throat, may also be involved.

Hysteric hemianesthesia presents the following features: It involves the left side much more frequently than the right; it is likely to appear suddenly, to be complete from crown to sole, and to terminate exactly in the median line of the body; it is usually accompanied by anesthesia of the mucous membranes and of the special senses on the side affected; it often disappears and reappears as suddenly as it began; and, finally, it may sometimes be transferred by suggestion from one side of the body to the other.

*Paresthesia* and *hyperesthesia* are also frequent in hysteria. Paresthesia, or perverted sensation, may take the form of numbness, flashes of heat or cold, tingling or burning, or the feeling of insects crawling over the skin. A very common paresthetic phenomenon is the so-called globus hystericus, which consists in the sense of a ball rising in the throat. Hyperesthesia often exists side by side with anesthesia. It is usually confined to the skin or a mucous membrane, but it may involve also the deeper structures. Very characteristic are the circumscribed areas of hypersensitiveness known as the hysterogenous zones. These are found most frequently in the iliac regions, about the mammary glands, along the spine, or over the sternum. Pressure on such areas may have the effect of inducing an hysteric paroxysm, particularly a convulsion, or, perhaps, of arresting a paroxysm if it has already developed. Of the mucous membranes, those of the vagina and urethra are most commonly affected, the result in one case being vaginismus and in the other, dysuria.

Closely related to hyperesthesia is spontaneous *pain*. This may take the form of rachialgia coccygodynia, hemicrania, or intercostal neuralgia. A well-known manifestation is clavus, an intense pain limited to a very small area of the head and likened to the sensation that would be produced by driving a nail through the skull. In rare instances the headache is accompanied by certain features suggestive of meningitis, such as vomiting and general hyperesthesia, and to this syndrome the term pseudomeningitis has been applied. In women the breast is occasionally affected, the gland becoming swollen, tense, exquisitely sensitive to touch and, perhaps, of a reddish or cyanotic hue. This condition, which is known as mastodynia, may follow trauma or intense emotion, or may be excited by menstruation.

In some instances inflammation of one of the larger articulations is closely mimicked. The affected joint, usually the knee or the hip, becomes painful, extremely sensitive, swollen, and often rigidily fixed. Other hysterical stigmata are usually present, the limb is not shortened, there is no atrophy of the muscles, the hyperesthesia is commonly more superficial and diffuse than in organic disease, and x-ray photography reveals no structural changes in the joint. Moreover, the rigidity often yields to mild force if the attention is diverted and almost invariably disappears under complete anesthesia. The possibility of hysteria being imposed upon an actual organic lesion must, of course, not be forgotten.

Finally, hysterical pain may more or less closely simulate angina pectoris.

*Special Senses.*—Of the organs of special sense, the eyes are most frequently affected. *Blindness*, partial or complete, is not rarely observed. It may develop suddenly or gradually and may be unilateral or bilateral. Amaurosis in the absence of any demonstrable lesions and with normal pupillary reactions is usually the result of hysteria. *Concentric contraction of the field of vision* and *inversion of the color field* (reversal of the the order and extent of the field for white and colors) are also fairly common, but are observed almost as frequently in brain tumor as in hysteria. *Tubular vision*, or contraction of the visual field to the same extent irrespective of the distance from the eye that the fixation point is placed, is almost pathognomonic of hysteria. Hysteric contraction of the field of vision is, as a rule, only disclosed on examination and rarely, if ever, interferes with orientation.

The senses of hearing, smell and taste are occasionally affected. Hysterical *deafness* and *loss of smell* (anosmia) are usually unilateral and are especially seen in association with hemianesthesia.

*Motor Disturbances.*—These include paralysis, contracture, convulsions, and tremors.

*Paralysis* is one of the most important of the hysterical stigmata. It may be limited to certain groups of muscles or even to individual muscles, or it may take the form of hemiplegia, paraplegia or monoplegia. It may be partial or complete, and may develop suddenly or gradually. Usually, it occurs in relation to trauma or emotional shock or follows a convulsive seizure. It may be transitory or it may persist for many years. The nutrition of the affected muscles, with rare exceptions, remains good; electric contractility is unchanged; and the tendon reflexes are normal or increased, but are never absent. The paralysis may be of flaccid type, but much more frequently it is attended by contracture. Anesthesia is also present in the majority of cases, but it does not always appear simultaneously with the paralysis and it rarely proves as persistent.

In hemiplegia, which is perhaps the commonest form of gross hysterical palsy, the face is rarely involved; Babinski's sign is always absent; true aphasia is never observed; the distal parts of the limb are often less affected than the proximal; and the arm lies flaccid at the side, while the leg is dragged, instead of being swung outward in a semi-circle, as in organic hemiplegia. In hysterical paraplegia the sphincters are not involved and there is no tendency to cystitis or to bedsores. Occasionally, the patient is able to make all of the movements of the lower limbs while sitting or reclining and yet can neither stand nor walk. This peculiar failure of coördination has been termed *astasia-abasia* (Blocq.).

Of the isolated hysterical palsies the most common is that which affects the laryngeal muscles and causes aphonia. Characteristic of the latter is the suddenness of its onset and the equal suddenness with which it may disappear. When the articulatory mechanism is completely paralyzed, as well as the phonatory, absolute mutism occurs. More rarely hysterical paralysis is observed in the muscles of the pharynx or neck. Hysterical ptosis may be the result of spasm of the orbicularis palpebrarum, but rarely, if ever, of palsy of the levator. Monocular diplopia not associated with any obvious lesion is usually hysteric.

Hysterical *contracture* usually, although not invariably, coexists with paralysis. Like the latter it may be confined to a single portion of a limb, as a hand or foot, or may be monoplegic, hemiplegic, or paraplegic. With the rigidity there is often anesthesia, but muscular atrophy is not observed, except in cases lasting many months or years. In contrast to organic con-

tracture, the hysterical form may yield to mild force if the attention is diverted, often disappears during sleep, and almost always relaxes during complete anesthesia.

In addition to contractures, *tonic spasms* limited to individual muscles or muscle groups often occur. In the neck these cause torticollis; in the esophagus, dysphagia; in the bladder, retention of urine; and in the abdominal-wall, the well known "phantom tumor."

The *convulsions* of hysteria bear a more or less general resemblance to those of epilepsy, but careful examination usually reveals a number of significant differences. Prodromes consisting of various emotional or mental phenomena, digestive disturbances, or an exaggeration of the more permanent symptoms of the disease (stigmata) are rarely absent, and immediately preceding the paroxysm there is often a definite aura in the form of the globus or clavus, or a sense of appression about the chest. The attack begins suddenly, the patient, if standing sinks to the floor, rather than falls, and at once becomes rigid. Consciousness may be impaired, but it is not entirely lost. The eyelids are partially closed and may be tremulous. There is no tendency, however, to squinting. Tonic rigidity may predominate throughout the attack, or clonic contractions, of wider range and more of the nature of coördinated movements than those of epilepsy, may supervene. No physical injury is sustained at the inception of the attack, the tongue is never bitten, no relaxation of the sphincters occurs, and the color of the face remains unchanged or becomes pale, but it never turns purple. The attack, which is usually of much longer duration than that of epilepsy, may result in exhausation, but it is never followed by deep sleep. Occasionally it ends in an outburst of sobbing or laughing, or in some other emotional display. At the close of the paroxysm there is in many cases a copious discharge of limpid urine. Not rarely the attack may be reproduced by suggestion or by pressure over an hysterogenous zone.

The "*grand*" *hysterical attack* described by Charcot and his colleagues of the Salpêtrière School is rare in America. In this form the usual epileptoid phenomena are followed by three other phases. In the first phase (period of "clownism") the body is forcibly twisted into some bizarre position as that of extreme opisthotonos or is kept in violent motion. In the second phase (period of passionate attitudes) the patient's facial expression, posture and gestures dramatically portray an intense emotion, as that of grief, joy, voluptuousness, penitence or religious ectasy. In the final phase (period of delirium) consciousness is less obtunded and speech takes the place of gestures and postures as a means of expressing emotion. The utterances correspond with the mental state and not rarely indicate actual illusions or hallucinations. Such an attack may last an hour or longer, or may recur in series extending over many hours (*status hystericus*).

Less frequent forms of hysterical motor excitation are *tremors* and *choreiform movements*. The former may simulate more or less closely the tremors of, chronic poisoning (alcohol, lead, mercury) or of disseminated sclerosis and the latter, the movements of St. Vitus' dance.

*Psychic Disturbances.*—The characteristic psychic feature of the hysteric is *abnormal suggestibility*. Indeed, the patient is so impressionable to suggestions arising both from without and from within his own organism that his will power is wholly inadequate to control reactions. In this way arise the well known paroxysms of immoderate laughter and weeping and other exhibitions of emotional instability, as well as the various somatic stigmata of the disease, such as anesthesia, paralysis, contracture, etc. Exceptionally,

the pathologic suggestibility is reflected in some peculiar modification of consciousness, as lethargy (semi-stupor), somnambulism (sleep wandering), or catalepsy, a condition in which the limbs present to passive motion a wax-like or "lead-pipe" flexibility, and remain for a long time in any position in which they are placed. Such phenomena are really but variants of one of the phases of the major attack, or *grande hystéria.*

Intentional simulation, morbid impulses, and even sexual perversions have also been ascribed to hysteria, but they are merely epiphenomena of exceptional occurrence, and have no place in the symptomatology of the disease.

*Visceral Disturbances.*—The digestive organs are affected in various ways. *Anorexia* or even intense disgust for food is sometimes observed and may be transitory or persistent. With it, or occurring independently of it, there may be obstinate *vomiting.* In many of the cases the emesis is not preceded by nausea, but occurs immediately after the food is swallowed, sometimes even before it has entered the stomach. Despite the vomiting the general nutrition often remains good for a long time; in some cases, however, extreme emaciation ultimately supervenes. In a few instances the vomiting has been fecal and associated with abdominal distention and complete constipation, as in intestinal obstruction. A patient under the care of Treves was operated on three times for supposed ileus.

Enormous *tympanitic distention of the bowel,* distressing *borborygmi,* noisy *eructations* of gas, and recurrent attacks of *singultus* may also occur in consequence of hysteria.

Disturbances of respiration are not infrequent. In some cases there is a persistent, dry barking *cough;* in others, there are attacks of intensely *rapid breathing* (60 to 80 respirations per minute) without cyanosis or acceleration of the pulse, and often without dyspnea, and not rarely there are prolonged *paroxysms of sighing inspiration* or of *exaggerated yawning.*

Apart from the pseudo-anginal attacks, to which reference has already been made, cardiac disturbances are not very common. *Hysterical tachycardia,* however, is occasionally observed. Urinary disorders are more frequent. *Polyuria* is especially noteworthy. It may occur at the end of a convulsive seizure and be transitory or it may occur as an interparoxysmal symptom and persist for a greater or less length of time. *Pollakiuria, retention* of *urine,* and *transient oliguria* or *anuria* are also met with, but reports of hysterical anuria lasting for many days must be accepted with reserve.

*Vasomotor and Trophic Disturbances.*—Disorders of vasomotor innervation are not uncommon. Of this nature are the sudden attacks of *flushing* or *pallor;* the alternating *sensations of heat and cold;* the *localized ischemia* of the tissues sometimes occurring with hysterical paralysis or anesthesia; the phenomenon known as *dermographia,* in which persistent red lines or urticarial streaks (urticaria factitia) are evoked by stroking the skin firmly with a hard, somewhat pointed object; and the peculiar *edematous swellings* occasionally seen in association with other stigmata, such as paralysis, anesthesia, or hyperalgesia, and not rarely accompanied by marked cyanosis and coolness of the overlying skin (Charcot's œdème bleu).

Recurrent attacks of *gangrene and spontaneous hemorrhage* into the skin or from the various mucous membranes have also been ascribed to hysteria, but there is reason to believe that in many of the recorded cases these conditions have been either fictitious or accidental. Slight *elevations of temperature* may occur, but they are exceptional, and it is certain that most, if not all, of the cases of alleged hysterical hyperpyrexia reported in medical literature have had their origin in malingering.

**Diagnosis.**—The diagnosis is usually easy in uncomplicated cases. In reaching it attention should be paid to the following points: (1) The history of the patient, particularly as it relates to heredity and temperament, and to the previous occurrence of similar attacks or of other indubitable hysterical phenomena; (2) the mode of onset, as for instance, the sudden development of the symptoms after emotional shock or suggestion; (3) the peculiar grouping or distribution of the symptoms, which is often incompatible with the existence of any organic lesion; (4) the marked mobility of the symptoms, that is, their variability in intensity from hour to hour or day to day, their tendency to shift, and, above all, their sensitiveness to suggestion; and, finally, (5) the exclusion of every form of organic disease that may bear any resemblance to the condition presented. In this connection it must not be forgotten that hysteria frequently occurs as a complication of *organic disease*, and that it is always unwise to assume the absence of the latter merely because a few hysterical symptoms form a part of the clinical picture.

The conditions with which hysteria is most likely be confused are neurasthenia, psychasthenia, hypochondriasis and dementia præcox. Although neurasthenia and hysteria sometimes coexist, the two neuroses are entirely distinct. *Neurasthenia* is a state of ready exhaustion, and is manifested by incapacity for sustained mental and physical exertion and by increased irritability. The patient complains of persistent fatigue, mental weariness, tachycardia upon slight effort, headache and pain in the back, tardy digestion, coldness of the extremities and other vasomotor disturbances, but such phenomena as anesthesia, exaggerated emotional expression, paralysis, amaurosis, convulsion and contracture are wholly wanting.

In *psychasthenia* the general symptoms of neurasthenia are sometimes present, but the mental features dominate the clinical picture. Mental tire, inability to fix the attention, slowness of thought, timidity, irresolution, a sense of vague apprehension and fear, not rarely developing into veritable phobias, are common manifestations, but none of the somatic or stigmatic signs of hysteria are observed. *Hypochondriasis* is a pure mental condition characterized by a fixed conviction of illness when such illness does not exist. The patient usually refers his symptoms to one or more of his organs and frequently his obsession is so pronounced that it dominates his life and becomes disabling. The true hypochondriac, however, presents neither the stigmata of hysteria nor the evidences of fatigue.

The differentiation of hysteria from *dementia præcox* is not always easy, as in the symptomatology of the latter there are often indubitable signs of hysteria. However, mental enfeeblement, emotional depression and indifference, actual delusions or hallucinations, outbreaks of wild excitement, impulsive actions manifested without purpose, senseless reiteration of words or phrases or repetition of movements (stereotypy), insusceptibility or obstinate resistance to normal influences (negativism) and inattention to the demands of nature are strongly indicative of dementia præcox.

**Prognosis.**—The outlook for complete and permanent cure is not good. While individual symptoms almost always disappear sooner or later under appropriate treatment or even spontaneously, the underlying constitutional condition is likely to continue through life or at least until old age. The risk to life is very slight. In a few instances death seems to have occurred from laryngeal spasm or persistent vomiting. The different manifestations vary in their amenability to treatment. As a rule, disturbances of sensation yield more readily than those of motion, hemiplegia, paraplegia and severe contractures being especially difficult to manage.

**Treatment.**—By proper mental, moral, and physical training much can be done to prevent the occurrence of hysteria in those who through inheritance are predisposed to the disease. Prophylactic treatment includes the inculcation of absolute obedience, self-restraint and self-denial, a judicious education, suitable outdoor exercise, hygienic surroundings, temperate living, and the avoidance of all that tends to morbid emotionalism or sentimentalism.

In developed hysteria treatment must be directed both to the mind and the body, but especially to the former. To be successful the physician must be able to inspire absolute confidence and faith in the mind of the patient. She must be impressed repeatedly with the fact that her condition is a curable one, and that with her thorough cöoperation restoration to health will certainly follow. To intimate that her symptoms are feigned or are wholly within her control is an egregious error. The physician's authority must be unquestioned and his instructions must be rigidly carried out. Want of firmness and of decision is a common cause of failure. Harsh measures are occasionally needed, but they should be adopted only after the most careful consideration. In many cases no method of treatment proves successful until the patient has been removed from her customary surroundings and separated from her sympathetic relatives and friends.

Suggestion is employed consciously or unconsciously in the treatment of hysteria by every successful physician. Without it most of the remedies recognized as efficacious become wholly impotent. The cures which are said to have resulted from the application of magnets and of various metals (metallotherapy) to the surface of the body are now known to have been due solely to suggestion. Complete hypnotism is by no means so generally useful as continuous suggestion. Certain symptoms—paralysis, aphasia, blindness, anesthesia—are sometimes removed by a single hypnotic séance, but on the whole, the action of hypnotism is disappointing. Moreover, in the event of failure, it is likely to lower still further the will-power and to increase the emotional instability.

According to Freud, hysterical manifestations cannot be successfully combated in many cases unless the patient's defensive inhibitions are removed by admitting to consciousness his suppressed reminiscences through a process of verbal reaction, and to accomplish this one must have recourse to psycho-analysis, which consists in a careful examination of each neurotic's sexual life history, even that of his early childhood, or, as Putnam expresses it, in an exorable scrutiny of the unconscious regions of his memories and thoughts, with particular reference to his sexual life. Much importance is attached also to dream analysis, for it is held by Freud and his followers that dreams are symbolic and reveal to those skilled in their interpretation the sexual aberrations and unsatisfied desires which in his waking moments the patient unconsciously suppresses. Doubtless, psycho-analysis has sometimes proved of service in hysteria, probably in ways other than those suggested by its author, but its practice had better be left to the trained psychologist, as in the hands of the unskillful it is certainly likely to do more harm than good.

The physical condition of the hysterical patient must not be neglected. In mild cases general measures, such as change of scene, graduated exercise in the open air, hydrotherapy and massage, usually suffice. In severe forms of the disease the treatment that is associated with the name S. Weir Mitchell (see p. 1035) often yields excellent results, but it is not always appropriate, and considerable judgment must be exercised in the selection of suitable subjects for it.

Apart from their psychic effect, drugs have little influence on hysteria. They must often be used, however, to meet underlying conditions and to combat special symptoms. Iron and arsenic are useful when there is anemia. Antispasmodics, such as valerian, asafetida, sumbul, and camphor, are sometimes helpful, probably in consequence of their impressive odor and taste. Occasionally, direct sedatives, such as the bromids, chloralamid, veronal, or acetphenetidin, may be required, but the continuous use of such remedies is always to be condemned. Powerful narcotics, such as morphin, chloral and alcohol, are decidedly dangerous.

When hysteria is complicated by local disease special treatment may be necessary, but no surgical operation should ever be performed merely in the hope of relieving hysterical symptoms.

*Convulsions.*—Isolation of the patient is imperative. Firm pressure over an hysterogenic zone, particularly one of the ovaries, is sometimes successful. The effusion of cold water on the face may be useful. Inhalations of amyl nitrite or even of chloroform may be employed, if necessary. Emesis induced by apomorphin has yielded good results in some instances. *Hyperesthesia* and *pain* often yield to electricity, light massage and cold douching. In the case of *paralysis* the patient should be instructed how to regain by long-continued practise the use of the affected part. This process of reëducation demands the exercise of great patience and firmness. Swedish movements, massage and faradization are useful adjuvants. *Aphonia* is often successfully treated by the faradic current, one electrode being placed over the larynx and the other over some indifferent point.

*Contractures* are best treated by passive movements, electricity and suggestion. In refractory cases with secondary changes in the tendons and fibrous tissues it may be advisable to straighten the limb forcibly under anesthesia.

## TRAUMATIC NEUROSES

**(Railway Spine; Shell Shock)**

The term "traumatic neuroses" was first used by Oppenheim in 1889 to designate the various functional nervous disturbances that not rarely make their appearance after an accident or injury. Erichsen originally drew attention to the symptom-complex in his monograph on "Spinal Concussion," published in 1871, although he did not recognize its real significance. As employed at the present time the term does not signify a disease *sui generis*, but a group of psychoneuroses or neuroses that develop in connection with accident or injury. In the large majority of cases the symptoms are those of pure hysteria; much less frequently the clinical picture is that of neurasthenia alone or of neurasthenia and hysteria combined; and occasionally the disturbances are essentially hypochondriacal.

In the **etiology** of these conditions psychic shock has a much greater etiologic significance than physical injury, which is often slight or even imperceptible. Indeed, terror or fear alone may produce identical disturbances, especially if the individual's mind is already prepared for them by environmental influences. The term "shell shock," originated during the World War, has been applied loosely to a number of entirely different nervous conditions occurring in soldiers, especially in men occupying the front-line trenches. The condition in some instances was due to actual concussion of the

central nervous system without visible injury (true shell shock); in the large majority of cases it was an expression of hysteria or of neurasthenia, and so was clearly allied to the traumatic neuroses; in a comparatively small group of cases it was one of hyperthyroidism from overstimulation of the nervous system; and occasionally it was a simulation of hysteria or of neurasthenia by a malingerer.

The occurrence of traumatic neuroses is especially favored by an innate neuropathic tendency. Commenting on shell shock, Mott[1] writes; "Of even greater importance than the extrinsic conditions in this causation of military unfitness from exposure to shell fire are the intrinsic conditions, for if there is an inborn timorous or neurotic disposition, or an inborn or acquired neuropathic taint, causing a *locus minoris resistentia* in the central nervous system, it necessarily follows that such a one will be unable to stand the terrifying effects of shell fire and the stress of trench warfare."

The **symptoms** of traumatic hysteria and neurasthenia do not differ materially from those of hysteria and neurasthenia arising from other causes. In the cases of shell shock that are strictly in the category of the traumatic neuroses the most common manifestations are temporary unconsciousness, or stupor, amnesia, terrifying dreams, motor paralysis, anesthesia, amblyopia, contraction of the visual fields, loss of taste and smell, mutism, tremors and various vasomotor disturbances, particularly cold blue hands and excessive sweating. The outlook in the traumatic neuroses depends on many factors, but especially on the severity of the preëxisting neuropathy and the character of the environmental conditions. In the majority of cases the symptoms eventually subside. It is well recognized that in hysterical cases involving the right to pecuniary damages a clinical cure rarely occurs until settlement has been made and litigation disposed of, and, therefore, from a medical viewpoint, it is usually advisable for the patient to end the matter as soon as possible by compromise.

## OCCUPATION NEUROSES

This term is used to designate certain motor disturbances produced by the constant repetition of movements requiring delicate coördination and manifested only in the performance of those particular movements.

Writers' cramp is the most common of these neuroses, but similar disturbances are also observed in telegraph operators, seamstresses, pianists, violinists, cigar makers, engravers, milkers, blacksmiths and professional dancers. Public speakers are sometimes affected in the muscles of phonation. Oppenheim regards the nystagmus of miners as belonging to this category. With regard to the etiology, much importance attaches to a neuropathic disposition, which may be hereditary or acquired. Males are more frequently affected than females and the great majority of sufferers are between the ages of 20 and 50 years.

The pathogenesis of the occupation neuroses is still obscure. That the underlying disorder is central (psychomotor neurosis) rather than peripheral is strongly suggested by the neuropathic history, the frequency with which the symptoms pass from one side to the other when the patient attempts to substitute the unaffected member for the affected one, and the fact that subjects of these neuroses almost always display other evidences of nervous instability. It is true, however, that signs of neuritis or of neuromyositis

[1] Brit. Med. Jour., 1917, 2, 39.

from over-use of the muscles or from pressure are also present in a small proportion of cases, but the two conditions, occupation neuritis and occupation neurosis, are quite distinct and should not be confused.

**Writers' Cramp** (**Writers' Palsy, Mogigraphia**).—This is caused by excessive use of the muscles of the hand and wrist in the act of writing. An awkward manner of holding the pen is of especial import. The symptoms usually develop gradually, a sense of fatigue or pain first appearing in certain muscles of the hand and arm shortly after the patient has begun to write, compelling him to rest for a time. Sooner or later in many cases spasmodic contraction of the muscles occurs when the penholder is clasped, so that the pen is irregularly jerked to and fro or is firmly driven into the paper (*spasmodic form*). In other instances spasm is replaced by muscular immobility, in consequence of which there is a tendency for the penholder to slip from the hand (*paralytic form*). Paralysis, although simulated, is not actually present, the patient being able to do work with the hand other than writing as well as ever. Occasionally tremor is the chief manifestation (*tremulous form*). Though the hand is quite steady when not being used in writing it begins to shake as soon as the pen is clasped. Coarser movements involving the muscles of the hand do not give rise to symptoms, but in exceptionally severe cases other activities than writing requiring fine coördination may induce similar disturbances. Pain, numbness, heaviness and other parasthesiæ are frequently noted in all forms of writers' cramp, but objective sensory changes are constantly absent unless there is an accompanying neuritis. The presence of other neuroses: neurasthenia, hysteria, tic, and neuralgia, is observable in many cases.

The *diagnosis* is usually easy. It must not be forgotten, however, that similar disturbances sometimes mark the onset of certain organic diseases of the central nervous system, such as chronic poliomyelitis, tabes, disseminated sclerosis, and cerebral apoplexy. In occupation neuritis the affected member is incapacitated for other work than that which has induced the disease, and there may be objective sensory symptoms, wasting of muscles, and changed electrical reactions.

The *prognosis* of writers' cramp should be guarded. Generally speaking only mild cases are susceptible of lasting relief. Whatever the plan of *treatment* adopted, the results are likely to prove more or less disappointing unless the patient refrains from writing for at least one or two years. Even under the most favorable conditions work can only be resumed slowly and gradually. Education of the left hand is desirable, although that member also is likely to become affected in time.

Writing is sometimes facilitated by using a light splint which has been shaped to the forearm and wrist and to which is attached a wooden ball fitted to the palm of the hand and carrying a penholder, or by thrusting the penholder through a large rounded cork that can be grasped by the palm and base of the thumb. The object of such contrivances is to substitute movements of the entire arm and shoulder for those of the fingers and wrist. A change of occupation, however, is the best treatment. The general therapeutic measures suggested for neurasthenia are usually indicated. Massage, hot and cold douches, and electricity (mainly for its psychic effect) may be beneficial. In some instances Bier's treatment—the application of an elastic bandage above the elbow for half an hour twice a day—appears to have been of service.

## MIGRAINE

(Megrim; Hemicrania; Sick Headache)

**Definition.**—Migraine is a neurosis characterized by recurring attacks of severe headache, which is usually unilateral or more marked on one side of the head and which is frequently associated with visual disturbances, nausea and vomiting and various paresthesias.

**Etiology.**—Migraine usually develops in childhood or in youth. It rarely begins after thirty. Females are somewhat more prone to it than males. Heredity is an important etiologic factor, the same affection or other neuroses being found in a direct or a collateral line of the ascendants with extraordinary frequency. A gouty family history can also be traced in many cases. In-door life and sedentary habits are favorable to the development of the disease. The association of migraine with epilepsy in the same individual has been frequently noted, but what relation the one affection holds to the other can only be conjectured. The exciting causes of the attack are various; among the most common are digestive disturbances, such as may arise from overeating or prolonged fasting, constipation, mental or physical fatigue, emotional excitement, eye strain, insufficient sleep, and lack of fresh air.

Concerning the nature of the disease most diverse opinons have been entertained. Liveing, Möbius, Gowers, Jackson and others believed the fundamental condition to be a constitutional defect of the cerebral cortex and that the attacks developed spontaneously (sensory epilepsy). Others have assumed that the primary factor is an intoxication of endogenous origin, and others still that the essential feature is a vasomotor disturbance conditioned by a variety of causes.

**Symptoms.**—*Premonitary symptoms*, lasting several minutes, a few hours, or occasionally one or two days, are usually present. The most common are a sense of weariness or of depression, yawning, chilliness, vertigo and some form of visual disturbance. Sometimes the premonition is distinctly agreeable, the patient regularly experiencing on the day before the attack a feeling of well-being or of actual buoyancy (euphoria). In other cases the headache is preceded by tingling or numbness in the arm, hand or lips, by subjective sensations of taste, or by tinnitus aurium. Occasionally, transitory hemiparesis or aphasia occurs before or accompanies the attack. Of all premonitions, however, the most common is some form of visual disturbance. In many cases a luminous spot appears near the fixing point and gradually enlarges to one side, presenting a zigzag form and a peripheral play of colors—the "fortification spectrum." Within it vision is blurred by the vivid scintillation. Instead of this flittering scotoma there may be dimness of vision, contraction of the visual field, or hemianopsia. The derangement of vision is usually bilateral, although at first it may be limited to one eye.

The *pain* varies considerably both in location and in intensity. It commonly begins above the eye or in the temple and spreads over the side of the head. The eye-ball is frequently sensitive to pressure. Sometimes the pain is limited to a small area in the frontal or parietal region, and occasionally it is occipital. It may be strictly unilateral, but in many cases it is felt on both sides of the head, although usually with greater intensity on one side than on the other. Some patients describe it as a dull ache, others as throbbing or boring in quality.

Bodily movement, loud noise, strong light, and mental effort almost always increase it, and for this reason many sufferers desire to be left alone in a quiet and darkened room. After a time, generally at the acme of the pain,

nausea supervenes, and, as a rule, culminates in vomiting, which usually affords relief and is often followed by sleep. Less frequently the pain abates gradually without vomiting. In some paroxysms chilliness, scotomata or other sensory phenomena, and nausea occur without headache (abortive migraine) and in others headache is the chief or only symptom.

In many migraine attacks *vasomotor disturbances* are prominent. Thus, there may be marked pallor, with a small pulse and coldness of the extremities; or there may be redness of the face, with a full pulse and a feeling of warmth, or these two states may alternate. An increase of the blood pressure is frequently observed during the paroxysms.

Drowsiness is common. It usually appears as the pain is subsiding, but it may come on at the height of the paroxysm and culminate in heavy sleep or a state of stupor. In some cases of migraine there are pronounced *psychic disorders*, such as confusion of thought, disturbances of speech, mental depression, hysteric phenomena, vague unsystematized delusions, or mild delirium. Liveing[1] in his classic monograph states that mental symptoms of one kind or another were present in one-fourth of his cases. *Secretory disturbances*, especially sweating, salivation and, at the close of the paroxysm, copious urination, are not infrequently noted. Occasionally the pain is accompaned by paresis of one or more of the ocular muscles (*ophthalmoplegic migraine* of Moebius[2] and Charcot[3]), or by hemianopsia, hemiparesis, aphasia, or even palsy of the facial nerve (facioplegic migraine). These focal manifestations are usually transient and are doubtless due to vascular spasm. In very exceptional cases, however, probably owing to thrombosis or actual rupture of a cerebral artery, the disability proves permanent. In young children migraine may be represented by feverish attacks with headaches, suggestive at times of meningitis.

The attacks usually last from 8 to 12 hours, although they may terminate within an hour or two or be prolonged for several days. Recurrence may be at more or less regular intervals, and as often as once in two weeks or once a month, or it may be at intervals of varying lengths and only in response to some definite exciting cause. In women the attacks frequently coincide with menstruation. Complete cure is rarely effected, but the disease is often alleviated by treatment, and in many instances it abates spontaneously after the fiftieth year. Occasionally, a severe intercurrent illness is followed by a cessation of the attacks.

**Diagnosis.**—Errors in diagnosis are not likely to occur except in atypical cases, but care must be taken to exclude the *headaches simulating migraine that may develop in chronic nephritis, cerebral tumor, syphilis of the brain, and paretic dementia.* In *ordinary headache* from various functional disturbances the pain is not heralded by visual or other sensory phenomena, vomiting rarely occurs, and there is less prostration. Certain bizarre forms of *epilepsy* bear some resemblance to migraine, but in the former there is loss of consciousness, the premonitory visual disturbances (auræ) are momentary, never prolonged as in migraine, headache is not an obtrusive feature, and if there is vomiting it occurs soon after the fit and not after the headache has lasted several hours.

**Treatment.**—In the interval between the attacks it is necessary to make careful search for the various forms of peripheral irritation that are known to have an unfavorable influence on the nervous system, such as gastro-intestinal disturbances, eye strain, etc., and to remove, if possible, any of these

[1] Megrim, Sick Headache and Some Allied Disorders, 1873.
[2] Berlin klin. Woch., 1884, No. 38, xxi.
[3] Progrès Médical, 1890, xii, 31.

that may be found. Especially important is it to limit the diet to simple easily digested food, and to exclude all articles that the patient has found by experience to disagree. Alcohol and tobacco are, as a rule, better avoided. An abundance of fresh air, daily sponge bathing, gentle exercise in the open air, and a quiet life are indicated. Constipation must be relieved by dietetic and hygienic regulations, or, if necessary, by the use of saline or vegetable laxatives. A mercurial aperient once or twice a month may often be prescribed with advantage. When there is pronounced intestinal stasis, thorough irrigation of the large intestine once a week with plain water is sometimes helpful. Medication between the attacks is not often effective.

Oppenheim reports good results from the prolonged use of arsenic. Thyroid extract in small doses is occasionally of service. When the attacks are especially frequent a combination of sodium salicylate (10 grains—0.6 gm.) with sodium bromide (15 grains—1.0 gm.), thrice daily, may afford considerable relief. If taken at the earliest premonition, nitroglycerin ($\frac{1}{100}$ grain—0.00065 gm.), a large dose of bromid, a full dose of caffein or a cup of strong coffee will sometimes abort an attack. Less frequently, a single large dose of sodium salicylate (20–30 grains—1.3–2.0 gm.), with a brisk cathartic, will have a similar effect.

*The Attack.*—The patient should be kept at rest in a quiet, darkened, well-ventilated room. Hot or cold applications may be made to the head according to individual preference. In some cases a sinapism at the back of the neck and a hot mustard foot-bath mitigate the pain. The application of menthol to the forehead and temples is also soothing. The most useful remedies are acetphenetidin, antipyrin, salicylic acid derivatives, bromids, caffein and cannabis indica. Various combinations of these drugs should be tried. Such a combination as the following sometimes affords relief:

℞. Caffeinæ citratæ..... gr. xx (1.3 gm.)
Antipyrinæ..... ʒiss (6.0 gm.)
Sodii bromidi..... ʒiiss (10.0 gm.) M.
Fiant chartulæ No. xii.
Sig.—One in water every two hours, if needed.

Cannabis indica is sometimes very useful, when a reliable preparation can be secured. Two drops of the fluid extract may be given every half hour until the pain abates or until slight dizziness or mental confusion appears. Even larger doses may be used, if necessary. Morphin should never be employed, except as a last resort.

## FAMILY PERIODIC PARALYSIS

The chief feature of this rare affection is flaccid paralysis of the voluntary muscles occurring in distinct paroxysms at irregular intervals, between which the patient is apparently in perfect health. The loss of power may be partial or complete, and localized or general. It usually begins in the legs and then spreads to the arms and trunk, but it may be confined to either set of limbs, to one half of the body, or even to the neck. The muscles of the face, eyes, and throat and the sphincters of the bladder and rectum escape. Respiration is sometimes embarrassed. The onset is almost always at night. The patient may retire in his usual health and wake in the morning unable to move hand or foot. The paralyzed muscles do not respond to electric stimulation and the tendon reflexes are abolished. The mind is almost invariably clear and sensation, apart from a feeling of numbness or heaviness,

is normal. Signs of cardiac dilatation are occasionally noted. The attacks last, as a rule, from 6 to 72 hours and recur at intervals of from a few days to several months, the number often decreasing toward middle age.

The disease is distinctly hereditary. Thirty-five of the 53 cases collected by Taylor[1] occurred in 3 families. The onset is usually in childhood or adolescence. The two sexes are equally affected. Fatigue, exposure to cold, or overindulgence in food may be the exciting cause of an attack. The nature of the affection is obscure. Slight degeneration of the muscle-fibers has thus far been the only significant finding; but whether this is primary, as in the dystrophies, or the effect of some special poison, possibly of autochthonous origin, it is difficult to determine. The occurrence of the muscular weakness in definite paroxysms suggests some relationship with myasthenia gravis and the periodic ocular palsies.

Until the appearance of Holtzapple's report[2] of a family group of 17 cases with 6 deaths, each in attack, the disease was regarded as not being dangerous to life.

**Treatment** is unsatisfactory. Strict hygienic and dietetic regulations must be instituted. Improvement has been observed under a low protein diet (Edsall and Means). In Holtzapple's cases potassium bromid—30 grains (2.0 gm.), with citrated caffein—1 to 2 grains (0.06–0.13 gm.), repeated in one or two hours, seems to have been of service, especially when given at the onset of an attack.

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# VASOMOTOR AND TROPHIC DISEASES

## RAYNAUD'S DISEASE

Raynaud's disease[3] is a comparatively rare form of vasomotor instability characterized by the occurrence of the various phenomena of frostbite (ischemia, venous stasis, active hyperemia, and gangrene), singly or in succession, in the projecting portions of the body, either without an obvious cause or in response to a degree of cold quite inadequate to cause such disturbances in normal individuals.

**Etiology and Pathology.**—The disease may occur at any age, but young adults are especially susceptible. It is most common in neuropathic subjects and more women are affected than men. Hereditary predisposition is occasionally recognizable. Exposure to cold has a decided influence, many patients being able to trace their first attack to working out of doors in frosty weather, to moving into a damp house, or even to bathing the hands in cold water. Violent emotion, fatigue, traumatism and acute infections, especially malaria, appear to have been contributory causes in some instances. Arteriosclerosis is often present, and probably favors the occurrence of Raynaud's disease, but it is not an essential factor.

Our knowledge of the pathology of the affection is very imperfect. No constant provocative lesion has been found. Raynaud's theory as to the manner in which the various phenomena are brought about is generally accepted. He supposed that the prerequisite for the development of the

[1] Jour. of Nervous and Mental Dis., Sept. and Oct., 1898.
[2] Jour. Amer. Med. Assoc., Oct. 21, 1905.
[3] Raynaud, "De l'asphyxie locale et de la gangrène symétrique des extrémités." Paris, 1862.

disease is an abnormal excitability of the vasomotor centers, and that spasm of the small vessels, provoked by the action upon the centers of various internal and external stimuli, most frequently of cold impressions, is the immediate cause of the symptoms.

**Symptoms.**—Several phases or stages may be recognized: *Local syncope, local asphyxia, active hyperemia,* and *gangrene.* The parts attacked by *syncope,* usually one or several fingers, more rarely the toes, ears, cheeks or nose, suddenly become white and cold. At the same time there is generally impairment of tactile sensation, with a feeling of numbness and stiffness, and also, in many cases, actual pain. Pulsation in the larger arteries of the part is, as a rule, perceptible. Although one side is often affected in advance of the other, the ischemia tends to become symmetrical. The attacks may terminate in a few minutes or may last for hours or even days, and may recur several times a day or only at intervals of weeks, months or years. Many patients suffer only in winter. In the mildest form of the disease (dead fingers) restoration is effected rapidly and without reaction. Frequently, however, a stage of *active hyperemia,* with burning and tingling, supervenes before the normal condition is resumed. In other cases the ischemia gives place to cyanosis or local asphyxia, the second stage of Raynaud's disease.

*Local asphyxia* (acrocyanosis) is usually, but not invariably, preceded by local syncope. Not rarely both conditions are present at the same time in different parts. The affected areas are of a variable shade of blue, sometimes almost black, cold to the touch, slightly swollen, and often bedewed with sweat. Subjectively, there may be itching, burning, pricking, or pain of any degree of intensity. In the distribution of the lesions and in the frequency of the attacks local asphyxia accords with local syncope, but asphyxia, as a rule, lasts longer than syncope, and occasionally it ceases to be paroxysmal and becomes more or less persistent.

The issue is twofold: the cyanosis may be followed by active hyperemia and a gradual return of the normal state, or it may culminate in gangrene, the third stage of Raynaud's disease.

*Gangrene* occurred in 68 per cent. of Monro's series of 176 cases.[1] It is preceded almost always by local asphyxia and in many instances also by local syncope. The favorite sites are the extremities of the limbs and the ears. Occasionally the nose, lips, and cheeks are affected. In one group of cases small blebs form on the cyanotic areas and break, leaving sloughing ulcers, which after a time give place to cicatrices. In other cases the cyanosis deepens until the part is perfectly black; then a portion of the dark area gradually becomes dry, hard and shrivelled, and is ultimately cast off. In both types there is usually severe pain, but exceptionally the process is painless. As a rule, the distribution is roughly symmetrical. The extent of the necrosis is generally slight compared with that of the asphyxia, but one or more digits or even a considerable part of one or both feet may slough off. After successive attacks the loss of tissue may be very extensive.

**Associated Conditions.**—Paroxysmal hemoglobinuria is not uncommon. It occurred in 6.1 per cent. of Monro's cases. As a rule, it appears synchronously with local asphyxia, exposure to cold being the usual excitant of both conditions. Other disturbances involving the vasomotor system are sometimes observed. Thus, patches of congestive mottling, of purpura, of rust-colored pigmentation (*tachetée*) may occur on the skin, or there may be outbreaks of urticaria or of fugitive edema, crises of abdominal pain, paroxysms of amblyopia or attacks of transitory hemiplegia, with or without aphasia. An association with scleroderma has been noted in a considerable

[1] Raynaud's Disease, T. K. Monro, Glasgow, 1899.

number of cases. The thickening and hardening of the skin may be confined to the fingers (*sclerodactylia*) or may extend to various parts of the body. Deformity of the nails and joint affections resulting in ankylosis of the phalanges also occur in some cases.

**Course.**—The attacks may cease spontaneously at any time, but in the large majority of cases they continue throughout life. Occasionally, the disease exhausts itself with one attack. The danger to life from the neurosis itself is small, although death sometimes results from extensive gangrene, persistent hemoglobinuria, or an apoplectiform attack.

**Diagnosis.**—There are a number of conditions associated with marked vasomotor changes or gangrene which at times must be carefully considered. *Frostbite*, for example, may present all the symptoms of Raynaud's disease, the only differentiating features of the latter in some instances being the paroxysmal tendency and the abnormal susceptibility to cold. *Syringomyelia* may give rise to very similar symptoms, but the gradual onset, progressive course, and presence of dissociative anesthesia, muscular atrophy, oculo-pupillary symptoms, scoliosis, arthropathies, painless whitlows and septic processes in and about the joints will usually clear up the diagnosis. *Erythromelalgia* sometimes simulates Raynaud's disease, but in the former pain and discoloration are greatly increased or are only present when the affected part hangs down, there is local elevation of temperature, sensation is preserved, all symptoms are aggravated by warmth and relieved by cold, and there is no tendency to gangrene. The form of *syphilitic arteritis* described by Jacoby,[1] Fox[2] and others may produce many of the phenomena of the phenomena of Raynaud's disease, but it is associated with the usual evidences of syphilis and commonly gives rise to an asymmetric gangrene. *Thrombo-angiitis obliterans* may be distinguished by the persistence of the sensory symptoms, the occurrence of intermittent claudication, the absence of pulsation in the arteries of the affected limb, and the involvement of the limbs in succession rather than symmetrically. Moreover, thrombo-angiitis obliterans shows a strong prediiection for the feet and occurs almost exclusively in Russian or Polish Jews.

*Senile gangrene, embolic gangrene, diabetic gangrene, tabetic gangrene, the gangrene of acute infections, gangrenous ergotism*, the multiple gangrene of the skin rarely seen in *hysterical subjects*, and the gangrene which occasionally develops with *cervical ribs* are not likely to come seriously into question.

**Treatment.**—It is requisite to avoid all influences likely to excite an attack. When cold is the chief excitant, residence in a warm climate during the winter months usually affords great relief. A regimen tending to increase the patient's vasomotor stability and resistance is also of prime importance; thus an abundance of fresh air, of sleep and of nutritious, easily digestible food, warm clothing, lukewarm salt baths, moderate outdoor exercise and gentle massage are to be recommended. General tonics, such as iron, arsenic, strychnin, and quinin are frequently indicated, but no medicines have as yet yielded very satisfactory results. Even nitroglycerin, from which much was expected, is of little value as a prophylactic, although in large doses it is sometimes of service in attacks of local syncope or asphyxia. In a few instances calcium lactate in large doses seems to have influenced favorably attacks of local asphyxia. Electricity in the form of the galvanic hand bath or high-frequency currents, if it can be tolerated, may favorably influence the vasomotor symptoms. The application of a tourniquet to the arm or leg, according as the fingers or toes are affected, although extremely

[1] N. Y. Med. Jour., Feb. 7, 1921.
[2] Jour. Cutan. Dis., Aug., 1907.

painful, may prove decidedly helpful (Cassirer, Cushing, Osler). Venous hyperemia by Bier's method is worthy of trial. Relief is sometimes afforded by moderate dry heat, lukewarm fomentations, or alternate hot and cold douches. Hot drinks are beneficial. For severe pain antipyrin or acetphenetidin may be tried, but morphin will often be demanded. In the treatment of gangrene the usual rules of surgery must be followed.

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## ANGIONEUROTIC EDEMA

**(Giant Urticaria; Quincke's Disease)**

**Definition.**—Angioneurotic edema is an affection in which circumscribed edematous swellings appear spontaneously on various parts of the surface of the body and on the mucous membranes, last from a few hours to a few days, and, as a rule, recur at intervals. It appears to be closely related to urticaria.

**Etiology.**—The disease, which is not very rare, is chiefly met with in early adult life, but it may occur at any age. Men are more frequently affected than women. A majority of the cases are in neuropathic individuals. An hereditary tendency is often observed. In five generations of a family cited by Osler more than 20 persons were affected. Digestive disturbances, overwork, emotional excitement, exposure to cold, or a local injury may be the immediate cause of an attack in a susceptible subject. Idiosyncrasy to certain articles of food is sometimes a factor and not rarely the condition appears to be an anaphylactic reaction to a particular form of food protein to which the patient is sensitized. Alcoholic intoxication and acute infections have also been mentioned as etiologic factors. In many cases no definite cause can be assigned for the attacks.

The **pathogenesis** of angioneurotic edema is obscure. Quincke[1] regards the condition as a vasomotor neurosis producing dilatation and increased permeability of the vessels, and this view, although it leaves much to be explained, is usually accepted. Török, Hari and other writers believe that urticaria is due to the action of irritants upon the blood-vessel walls, and it may be that angioneurotic edema has the same pathogenesis.

**Symptoms.**—The swelling appears rapidly, often suddenly, and soon produces a feeling of tension, sometimes with marked itching. It lasts a few hours or a few days and then disappears almost as quickly as it came. The affected area may be but a few centimeters in diameter, or it may be the size of a saucer or even much larger. As a rule, it is well defined. Pressure of the finger may or may not cause pitting. In some cases the overlying skin is pale and translucent, in others it is pink or red. As regards the localization of the lesions, the face and extremities are the favorite sites. Of 36 cases analyzed by Quincke[2] the face was affected in 80 per cent. The genitalia are not rarely affected. In more than half of the cases the mucous membrane of the digestive tract or that of the upper respiratory tract is involved either alone or with the skin. Sometimes the tongue and uvula swell to enormous proportions. Gastrointestinal symptoms were present in 34 per cent. of the 72 cases collected by Collins.[3] Intense colic, meteorism, vomiting, diarrhea and even melena have all been observed, and in a number of instances the picture has so closely simulated that of appendicitis, intussus-

[1] Monatsh. f. prakt. Dermat., 1882, No. 5.
[2] Berlin Med. Klinik., 1921, xvii, 675.
[3] Amer. Jour. Med. Sci., Dec., 1892.

ception or perforation of a-peptic ulcer, that laparotomy has been performed. Edema of the larynx occurred in about 7 per cent. of Collins' cases. It produces marked dyspnea and occasionally it is the immediate cause of death (Osler, Griffith, Mendel, Morris).

The condition known as *intermittent hydrarthrosis* is also regarded by some authorities (Schlesinger, Cassirer, Garrod) as a special localization of angioneurotic edema. It is characterized by recurrent effusion into the joints, almost invariably the knees, without, as a rule, redness or fever. Many patients with Quincke's disease display other signs of vasomotor instability (*vasomotor ataxia*), such as urticaria, dermographism, transitory erythema, and epigastric throbbing, or a tendency to palpitation, vertigo or syncope. An association with or a transition into *visceral* (Henoch's) *purpura* is not infrequently seen and a combination with exophthalmic goiter or Raynaud's disease is occasionally noted.

Only when the gastrointestinal symptoms occur independently of the cutaneous lesions is difficulty in diagnosis likely to arise. *Hysterical edema* is usually associated with sensory or motor disturbances, is more persistent, and generally affects one of the conventional divisions of the body, as a breast, an arm, or a hand (glove-form). *Milroy's hereditary edema* affects only the legs and is permanent. The course of angioneurotic edema is very uncertain. In many cases the attacks recur at intervals for years or decades. Occasionally death ensues through edema of the larynx.

**Treatment.**—Removal of the cause, if it can be discovered, is of the first importance. Careful regulation of the diet and the maintenance of free action of the bowels, preferably with salines, sometimes give good results. In obscure cases quinin, calcium chlorid, antacids, and especially salicylates are the remedies most worthy of trial. In a case occurring in a syphilitic, reported by Burr,[1] a dose of arsphenamin effected a permanent cure. Severe gastrointestinal symptoms may require the external application of heat and the administration of morphin and atropin, and edema of the larynx, spraying with a solution of epinephrin (1 : 10,000) scarification, or even tracheotomy.

## ACROPARESTHESIA

The term acroparesthesia has been applied to a peculiar sensory disturbance consisting of tingling, numbness, and a feeling of stiffness in the distal portions of the extremities, chiefly the fingers, hands and forearms, and only exceptionally accompanied by objective changes. Occasionally, complaint is made of actual pain and rarely the paresthesia is associated with impaired sensibility and pallor of the skin or a slight grade of cyanosis, indicating a transition to Raynaud's disease. As a rule, the symptoms occur in paroxysms, which occur most frequently in the early morning hours (waking numbness) and which last from a few minutes to several hours.

Acroparesthesia occurs usually between the ages of 30 and 60 years and is much more common in males than in females. Of Cassirer's[2] 162 cases only 12 were in men. Overuse of the hands and constant irritation by cold water, as in washing or scrubbing, are important etiologic factors. The influence of the climacterium is sometimes apparent. The pathology of the disease is not definitely known. The disturbances are probably referable, however, to

[1] Jour. Nerv. and Ment. Dis., July 12, 1912.
[2] Die Vasomotorisch-trophischen Neurosen, Berlin, 1901.

irritation of the sensory nerve-endings caused by changes in the peripheral circulation. The symptom-complex itself is easily recognized, but the question whether it is present in a given case as an independent neurosis or as a preliminary manifestation of some organic disease of the nervous system, such as tabes or polyneuritis, or some general disorder, such as arteriosclerosis, myxedema or acromegalia, is occasionally perplexing. Pure forms of *Raynaud's disease* may be distinguished by the presence of pronounced vasomotor disturbances and the influence of cold in producing the attacks. In *erythromelalgia* the affected parts, usually the feet, are red, hot and painful, especially when they hang down or are pressed upon. In *neuritis* the paresthesia is limited to the distribution of certain nerves, is more constant, and is associated with pronounced objective phenomena. Paresthesia due to changes in the spinal cord secondary to *severe anemia* is, as a rule, readily excluded. Differentiation from *occupation neurosis* is sometimes difficult.

**Treatment** is often ineffectual. It consists in avoiding the deleterious influences likely to cause the disturbance, and in employing measures that tend to increase the patient's resistance. Tonics, hydrotherapy, massage, and electricity (galvanism, static spark, high frequency currents, faradic brush) are sometimes of service. Among special remedies that seem to have been beneficial in individual cases may be mentioned bromids, iodids, ergot, quinin, and thyroid extract.

## ERYTHROMELALGIA

This rare condition, first accurately described by Weir Mitchell[1] in 1878, affects chiefly the extremities of the body, the feet more frequently than the hands, and is characterized by burning pain, reddening of the skin, throbbing of the arteries, elevation of temperature and moderate swelling, especially when the affected limb hangs down or is used. Sometimes even slight pressure or exposure to heat will bring on an attack. Elevation of the limb, rest, and cold afford more or less relief. The pain is usually accompanied by hyperesthesia, and not rarely local hyperidrosis is also observed. In long-standing cases the redness may give place to a purplish or bluish tint and the muscles of the part may undergo atrophy. Gangrene probably never occurs. The disturbances may be confined to one member or even to the region of a single nerve. Of 67 cases collected by Cassirer both feet were affected in 24, both hands and feet in 17, one foot in 9, both hands in 2 and one hand in 1.

Erythromelalgia may occur at any age and in either sex, although men are somewhat more frequently affected than women. Prolonged exposure to cold, overexertion, and trauma are mentioned as predisposing causes. It may develop as an independent affection or it may occur in association with organic diseases of the central nervous system, for example, disseminated sclerosis, tabes, syringomyelia, and spinal tumor. A transition to Raynaud's disease is sometimes observed, and occasionally similar disturbances occur with chronic splenomegalic polycythemia (Schmidt, Parkes Weber). As to the nature of the process, little is definitely known. Changes have been found in the posterior roots, peripheral nerves and small arteries, but the reports are not concordant. The evidence at hand suggests a morbid irritation of the vasodilator fibers, the result in one case of inherent instability of the vasomotor centers, and in another, of organic changes in the peripheral nerves or in the spinal cord itself. Some cases simulate *thrombo-angiitis*

[1] Amer. Jour. Med. Sci., July, 1878.

*obliterans*, but this affection, which is dependent upon definite changes in the arteries and which occurs almost exclusively in young Jews, may be distinguished by the occurrence of intermittent claudication, the disappearance of the pulse in the affected vessels and the marked tendency to gangrene. When the symptoms are confined to one hand, the presence of a *cervical rib* must be excluded. The differentiation from typical cases of *Raynaud's disease* is not difficult (see p. 1051).

The **course** of erythromelalgia is usually very protracted. Occasionally spontaneous cure occurs. **Treatment** is unsatisfactory. Applications of methyl salicylate and menthol sometimes afford temporary relief. Electrotherapy in the form of both the faradic and the galvanic current has been commended. Kanoky and Sutton[1] report benefit from brief exposures to x-ray. Realizing the futility of milder measures Mitchell advocated nerve-stretching, or, if this failed, neurectomy. Cassirer[2] also recommends nerve-stretching in refractory cases, but the results of operative treatment have not been especially brilliant.

## SCLERODERMA

This is a rare disease resulting in a diffuse or circumscribed induration and atrophy of the skin and subcutaneous tissue. The skin becomes hard, tense, immobile, and so tightly bound to the subjacent structures that it cannot be pinched up in folds. Late in the disease it is thin and parchment-like. When the face is involved the hidebound features give the appearance of an expressionless mask. Muscles, joints and bones often share in the atrophic changes. Occasionally, the myosclerosis spreads beyond the superficial lesions into regions in which the skin is still free. Stiffness and deformity of the joints are frequently observed and may be due to hardening and shrinking of the periarticular tissues or to progressive changes resembling rheumatoid arthritis. Occasionally, the bones undergo atrophy. Abnormal pigmentation of the skin, sometimes so marked as to suggest Addison's disease, is present in many cases. Secretory disorders, particularly hyperidrosis, may accompany the trophic changes. Vasomotor symptoms are common, especially at the onset. Thus, for weeks or months before any induration can be detected there may be erythema, with swelling which does not pit, or vascular disturbances with color changes, exactly like those of Raynaud's disease. Sensory phenomena may be entirely absent, but not rarely paresthesia and articular pains are present in the early stages. Ulceration about the nails or knuckles occurred in more than 10 per cent. of 420 cases collected by Lewin and Heller.[3] The sclerodermatous changes may be diffuse, involving a large part of the body or in irregularly distributed patches or bands. In some instances the patches are limited to the region of certain nerves or spinal segments. One form of the disease (*sclerodactyly*) affects chiefly the hands, or rarely the feet, and is characterized by atrophy, absorption, and eventual disappearance of the terminal phalanges, and induration of the skin and stiffness of the joints. In another form known as *morphea* the induration appears on the trunk or face as discrete ivory-like patches surrounded by a zone of congestion or brownish pigmentation. An association with Raynaud's disease is somewhat frequently observed. Either

[1] Jour. Amer. Med. Assoc., Dec. 19, 1908.
[2] Die Vasomotorische-trophischen Neurosen, Berlin, 1901.
[3] Die Sclerodermie, Berlin, 1895.

affection may exist by itself for a time and then be complicated by the supervention of the other. Chronic arthritis, sometimes antedating the cutaneous changes, is not uncommon. Occasionally, an association with Graves' disease or facial hemiatrophy has been noted.

The **course** of scleroderma is, as a rule, chronic, but it may be acute, especially in children. Cases lasting fifteen or twenty years, with varying periods of progression and betterment, are not uncommon. Restoration is not very rare in morphea, but it is exceptional in the diffuse forms. The outlook is somewhat better in children, even in the acute cases. Death is usually due to intercurrent disease. Occasionally spontaneous arrest of the process occurs.

**Etiology.**—Neither the essential cause of the disease nor the primary pathogenic influence concerned in its production is definitely known. Exposure to cold and damp and psychic shock are mentioned as predisposing factors. In a number of instances one of the acute infections has preceded the onset. A majority of the cases are in persons in the third and fourth decades of life, but no age is exempt. Women are more frequently affected than men (2 to 1).

While scleroderma is usually regarded as a trophoneurosis, the suggestion that it is a perversion of nutrition which is analogous to myxedema and due to some disturbances of internal secretions cannot be ignored.

**Morbid Anatomy.**—The important changes are in the corium and subcutaneous tissues. Microscopic examination reveals flattening of the papillæ, hyperplasia and condensation of the connective tissue, increase of the elastic fibers, and sclerosis of the smaller vessels.

**Treatment.**—Treatment is unsatisfactory. Arsenic, iron, quinin and other tonics are useful in some cases. In a few instances thiosinamin has given encouraging results (Hebra, Kaposi, Gärtner). It may be administered subcutaneously two or three times a week, in doses of 1 to 2 grains (0.06–0.13 gm.) dissolved in warm glycerin (10 per cent.), or by the mouth twice a day, in doses of 1 to 3 grains (0.06–0.2 gm.). Of other drugs that have been recommended from time to time, thyroid extract in doses of from 1 to 3 grains (0.06–0.2 gm.), two or three times a day, is worthy of trial. Locally, warm baths, massage with oily preparations, and electricity in the form of local or general galvanization or high frequency currents are sometimes decidedly helpful. Roentgen-ray treatment has not rarely proved useful, especially in the circumscribed form of the disease (morphea). Neumann speaks favorably of hot-air treatment.

# DISORDERS DUE TO EXCESSIVE HEAT

## HEAT STROKE

Exposure to excessive heat, natural or artificial, may result in one of three conditions: (1) *Thermic fever*, (2) *heat exhaustion*, or, more rarely, (3) *heat cramps*. In thermic fever there is a high temperature, often hyperpyrexia, with more or less pronounced nervous symptoms; in heat exhaustion, a low temperature, with depression, sometimes collapse; in heat cramps, no thermal disturbance whatever, fibrillary twitchings and painful spasms of the muscles being the principal feature.

**Etiology.**—Heat stroke in any of its forms is observed chiefly in the hottest months of the year. The essential cause of the condition is prolonged exposure to excessive heat. Thermic fever (sunstroke, insolation) is usually due to exposure to the sun's rays, although it may result from indoor heat. There is no evidence that the actinic rays in sunlight play any part in causation. Heat exhaustion and heat cramps occur commonly among laborers who work in furnace-rooms, foundries, bake-shops, sugar refineries, mines, etc., but they may be produced also by exposure to the sun's heat. By interfering with heat loss through evaporation, a high degree of humidity and still air make high temperatures especially dangerous. Important predisposing causes are lack of acclimatization, poor ventilation, over crowding, heavy clothing, lowered vitality, muscular fatigue and overindulgence in alcohol. A temperature of 115°F. or higher in a dry breezy atmosphere is often well borne by vigorous healthy persons who lead temperate and well regulated lives. The large majority of cases of heat stroke occur in the third, fourth and fifth decades of life. Males, because of their more frequent exposure, suffer in greater proportion than females. White races are more susceptible than colored.

**Morbid Anatomy and Pathogenesis.**—Opportunities for postmortem studies are rare except in cases of *thermic fever*. In this condition the following alterations are commonly found: General venous congestion; edema of the leptomeninges, brain, and lungs; cloudy swelling of the liver, kidneys and heart; and capillary hemorrhages in the brain, mucous membranes and skin. Microscopically, the nerve-cells of the brain, medulla, spinal cord and posterior spinal ganglia show evidences of degeneration, the chromatic bodies of Nissl being especially affected (Van Gieson, Ewing, Steinhausen). The *pathogenesis* of thermic fever is obscure. Apparently an important factor is the retention in the body of certain protein poisons arising from altered metabolism. Whether the fever itself is produced by this intoxication or is a direct result of the breaking down of the heat regulating mechanism by the high temperature and excessive humidity is not known. However produced, the fever in turn adds to the general metabolic disturbance by increasing the oxidation processes. Secondary gross lesions, such as capillary hemorrhages in the medulla and edema of the meninges and brain, are probably responsible for some of the nervous manifestations observed in the more severe cases.

In *heat exhaustion* the changes must be less profound. Apparently vasomotor depression with congestion of the splanchnic vessels and depletion of the brain and superficial tissues is the chief feature. *Heat cramps* are probably due to degenerative changes in the muscles themselves, for they have been observed in limbs that were paralyzed as a result of acute poliomyelitis (Weisenburg). It has been shown by Kühne, Halliburton and others that certain muscle proteins coagulate at temperatures below those sometimes observed in sunstroke.

**Symptoms.** *Thermic Fever.*—The onset may be abrupt, but more frequently there are for some hours or even days before the attack certain premonitory symptoms, such as headache, dizziness, restlessness, malaise, nausea or vomiting, diarrhea, great thirst, and frequent micturition. The actual attack is ushered in with coma, or, less commonly, with stupor accompanied by delirium. With the coma or stupor there are often focal or general convulsions of the clonic or tonic type. The temperature may rise to 106°, 108°, or even 114°F., but in many cases it does not exceed 103° or 104°F. The face is flushed, the eyes are suffused, the skin is livid and usually hot and dry, although after a fall in the temperature it may be cold and clammy. Subcutaneous petechiæ are sometimes present. The pupils may be either contracted or dilated. The pulse is frequent and in severe cases, small, weak and irregular. The respiration is more or less labored, not rarely stertorous, and auscultation of the chest frequently reveals coarse moist râles. Vomiting is common and involuntary evacuation of the bowels is the rule. The urine is scanty and usually contains albumin and hyaline and granular casts. Glycosuria is occasionally observed. The blood may show microscopically a moderate leucocytosis and chemically, according to Gradwohl and Schisler,[1] a high retention of the non-protein nitrogen constituents. The cerebrospinal fluid is usually clear and increased. An excess of cells in it, polymorphonuclear at first and mononuclear later, has been noted by a number of observers (Dopter, Huble and Pigache, Dufour and Römer). Death may occur within an hour, but usually it is postponed for at least 12 or 24 hours. It may be due to asphyxia or cardiac failure. Even after the temperature has returned to normal and consciousness has been regained a fatal relapse may occur.

In some series of cases the mortality has exceeded 40 per cent. Unfavorable features are prolonged coma, extreme hyperpyrexia, recurring convulsions, active delirium, and, according to Gradwohl and Schisler, high retention of the nonprotein nitrogen constituents of the blood (creatinin around or above 5 mgm.). In favorable cases recovery may be rapid and complete. After the more severe forms of sunstroke, however, there not rarely remain permanently signs of brain injury, such as persistent headache, failure of memory, disturbance of speech, partial or complete paralysis, epilepsy, ataxia, dementia and various psychoses or neuroses. A very common sequel is a markedly increased susceptibility to heat.

*Heat Exhaustion.*—The mildest form of this condition is characterized by headache, vertigo, pallor, a sense of weakness, and faintness. In severe cases there is marked prostration or even actual collapse. The surface is pale, cold, and clammy, and the pulse is frequent and small. The temperature may fall as low as 95°F. Consciousness may be maintained, but not rarely there is delirium. Occasionally there are muscular cramps. The outlook is good under appropriate treatment.

*Heat Cramps.*—The chief feature of this condition, which was first described by Edsall,[2] is the occurrence of painful tonic spasms of the

[1] Amer. Jour. Med. Sci., Sept., 1917.
[2] Amer. Jour. Med. Sci., Dec., 1904.

muscles, notably those of the extremities and abdomen. Generalized fibrillary twitchings sometimes precede the cramps. The attacks occur spontaneously or in response to slight mechanical stimuli, last a minute or two, and subside, as a rule, within 24 hours. The prognosis is usually good, although some deaths have been reported.

**Diagnosis.**—The diagnosis of thermic fever is largely based on a knowledge of the exposure to heat and the occurrence of high bodily temperature. In some instances other conditions productive of coma, particularly cerebral apoplexy, uremia, and the cerebral form of pernicious malaria, may have to be considered. Heat exhaustion and heat cramps are, as a rule, easily recognized.

**Treatment.**—In prophylaxis much importance attaches to maintaining the bodily health and vigor by avoiding over fatigue and alcoholic and other excesses. The food should be sufficiently nutritious, but light and unstimulating. The clothing should be light and loose. Cold water should be taken freely. Cool or cold baths should be used frequently.

In *thermic fever* immediate reduction of the patient's temperature is essential. This is best accomplished by a cold bath to which ice is added, but if this is not available cold affusions may be employed or the body may be rubbed with pieces of ice. An ice-cap should be kept on the head. Ice-water enemas may also be administered. Whatever its form, the cooling process should be discontinued when the thermometer in the mouth registers 101°F., as the temperature usually continues to fall after the patient is removed to bed. Antipyretic drugs, such as acetphenetidin and antipyrin, are, as a rule, better avoided, although they may be used cautiously if the means of applying cold are not immediately at hand. The antipyretic treatment must be repeated whenever the high temperature recurs. Venesection (200 to 400 c.c.) is often of value in the asphyxial form, indicated by lividity, distention of the veins, and signs of pulmonary edema. Weakness of the pulse need not be regarded as a contraindication, as the circulation often improves with the abstraction of blood. Supplementary proctoclysis with normal saline solution may be of service. In some cases lumbar puncture is even more useful than venesection. Marked circulatory depression should be met by the use of stimulants, preferably caffein-sodium benzoate, camphor and strychnin, failure of respiration by artificial respiration, and convulsions by the administration of sedatives (bromids, chloral, morphin). Light nourishment should be given at somewhat frequent intervals and the bowels kept active by the use, if necessary, of mild salines.

The treatment of *heat exhaustion* consists in the use of external heat, the hypodermic injection of stimulants (caffein, camphor, strychnin, and digitalis), and, in severe cases, hypodermoclysis or proctoclysis with normal saline solution. For the relief of *heat cramps* warm baths and hypodermic injections of morphin are recommended. In the more severe cases, Welsh[1] has used apomorphin, in doses of $\frac{1}{20}$ to $\frac{1}{12}$ grain (0.003–0.005 gm.), with pronounced success.

[1] Jour. Amer. Med. Assoc., April 10, 1909.

# INDEX