CONTRIBUTIONS TO MEDICAL AND BIOLŒGICAL RESEARCH

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VOLUME TWO

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CONTRIBUTIONS TO MEDICAL AND BIOLOGICAL RESEARCH

DEDICATED TO

SIR WILLIAM OSLER

BART., M. D., F. R. S.

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REHABILITATION OF THE DISABLED

By Frank Billings, M.D., Washington, D. C.

THE World War has aroused an universal interest in the physical and mental rehabilitation of disabled soldiers. The instruments of destruction of modern warfare sacrificed so many lives and disabled such a multitude of men that it became necessary to utilize all possible measures to conserve man power. There was urgent need to hasten and to make more certain the restoration of the soldier disabled by illness or wounds so that he could return to military duty.

Modern military medicine and surgery is a development of the World War. It is efficient. Phenomenal technical surgical skill and wise and rational medical management contemplate functional as well as physical restoration. The armamentarium of the military medical officer embraces in addition to the knife and drugs, hydro-, electro-, and thermo-therapy; passive and active exercise in the form of massage; of curative work both manual and mental in wards, shops, gardens, and fields; of drill, calisthenics, and physical culture, and of sports and pastimes in and out of doors.

These measures hasten and make more certain the recovery of the disabled soldier. Their application maintains the constant interest of the medical officers, nurses, and enlisted personnel in the welfare of the patient. It diverts the mind of the disabled man from the contemplation of his present suffering and future fate; the morale of the hospital corps and the patients is kept at a high standard.

Based upon available statistics, from 80 to 85 per cent of combat-injured soldiers of the allied armies returned to combat duty. From 5 to 10 per cent of combat-disabled soldiers, unfit for full military service, returned to special or limited duty. Of the remainder, unfit for all military service, continued treatment was carried to the fullest degree of restoration possible when the nature of the disability is considered. These disabled men unfit for all military service include the blind, the deaf, the dismembered, the severely gassed, the insane, and others. Among these must be classed also those disabled by illness, including tuberculosis, meningitis, chronic nephritis, organic heart disease, epilepsy, insanity, and other morbid conditions.

Practically all of the countries engaged in the war have endeavored, with more or less success, to extend the attempt at physical and functional restoration of the disabled soldier no longer fit for military duty, beyond the period of the needed hospital care. This involves a program of education and training to overcome the permanent physical handicap and to fit them to become self-sustaining economic factors in civil life.

The blind are no longer left to brood and lament to the degree of mental degeneracy. The remarkably efficient school for the blind at St. Dunstan's, organized and directed by Sir Arthur Pearson, has set an example which will hereafter force all civilized governments properly to educate and train the adult population blinded in industrial occupations or by disease. Under the Medical Department of the U. S. Army, a school for the blinded soldiers and sailors modeled upon St. Dunstan's is maintained at U. S. General Hospital No. 7, Baltimore.

In like manner deaf soldiers are taught lip reading, and speech defects are corrected by proper training. Coincidentally, the disabled soldier is educated and trained better to qualify him for his old occupation or for a new and gainful trade or profession.

The soldier who suffers from an improvable type of tuberculosis is given a form of curative work, either manual or mental, which will divert him and aid in the avoidance of hospitalization. The convalescent tuberculosis patient is especially benefited by work in the open air, on a protected porch, or in garden or field. Intelligent medical supervision as to the dosage of work and a common-sense choice of practical forms of curative work are essential in the treatment of the tuberculosis patient.

The object of the training and education of dismembered patients is two-fold. First, the training of the brain and of the muscles of the remaining limb or limbs is for the purpose of making the one limb perform the function of two. The left upper extremity may be trained to do all and more than the lost right arm did. Properly fitted artificial legs may become, with supervised and regulated rational practice, almost as useful as the natural ones. Second, training or education for life employment, which may be carried on coincidentally with the efforts to restore control of a member or to attain what may be termed vicarious function.

One may not contemplate the physical and mental rehabilitation of disabled soldiers without a consideration of the past and present neglect of the disabled men in the great industrial armies of the world. It has been stated that 750,000 people are injured annually in the industrial occupations of eighteen of the United States of America. That 35,000 of these individuals are permanently disabled. It is also stated that of people engaged in industrial occupations, 80,000 are permanently disabled annually in the whole United States. Of these, 2000 are totally disabled. This enormous crippling or entire loss annually of the industrial workers must be met by a policy of conservation and a rational program of rehabilitation of the disabled. The experience of the allied countries associated in the World War in the rehabilitation of disabled soldiers should be applied to the disabled of the industrial army.

The policy of rehabilitation of the disabled should be the same as that applied in military organizations, but the program should be modified to meet civilian demands and conditions. During the conflict disabled soldiers were kept in the hospital or in convalescent training centers until fit for military service. The military authority trained and educated the disabled soldier, no longer fit for combat service, for special or limited military duty. Then it was necessary to organize educational and trade-training facilities at the military hospital, which was, necessarily, more or less an educational institution.

In civil life, the chief function of the hospital is to afford the patients the most efficient methods of medical and surgical care and the most certain and rapid physical and functional restoration with due consideration of the nature of the disability. To facilitate the *physical* and *functional* restoration of the patients, the hospital

must furnish efficient, medical, surgical, and nursing care, adequate facilities for physiotherapy, for occupational therapy, and for play and other amusements. Occupational therapy must be applied primarily for the purpose of functional cure, but the rational choice of forms of curative work, at the bedside, in shop, or elsewhere, may be essentially pre-vocational, or even the primary steps of vocational training. The more nearly curative work approaches occupational training, the greater the therapeutic value, because of the gain in useful knowledge and the consequent interest the patient takes in the work as a rule.

Many disabled industrial workers will need training and education to overcome the handicap of a permanent disability. This training and education is not a function of the hospital. The hospital has discharged its responsibility when the treatment of the patient has reached the stage of the completed physical and functional restoration consistent with the nature of the disability. But the disabled industrial worker should have the opportunity for this training and education. If he takes advantage of the opportunity, the training and education will neutralize the handicap due to the disability. He may then return to his old or to a new job an efficient economic factor in the industrial world, instead of an unhappy dependent of the government or state.

The policy of rehabilitation of the disabled and, by the practice of it, the conservation of man power and of individual and community self-respect and happiness, is imperatively demanded. Provision for its universal efficient application must be made by the government, either Federal, State or Municipal, or by all co-operatively.

Pensions and disability compensation are just measures for the relief of permanently disabled soldiers and injured industrial workmen. These measures of financial relief should be continued as additional aids in the attempt to provide efficient rehabilitation of permanently disabled victims of war and of accidents due to industrial activities.

The efficient application of the complete rehabilitation of permanently disabled soldiers and men and women of the industrial army will materially lessen the inmates of soldiers' homes and of almshouses. Only those soldiers and civilians whose disabilities are total will seek refuge therein.

THE CHOICE AND TRAINING OF MEDICAL OFFICERS FOR THE AIR FORCES

By Thomas R. Boggs, M.D., Baltimore, Md.,

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FROM the most ancient times medical men have been interested in the theoretical and speculative aspects of flying, and now that the development of modern warfare has brought hundreds of doctors into contact with what is for them an unexplored field of professional activity, and practically forced the evolution of a new specialty, it may seem not altogether inappropriate to discuss briefly some points bearing on the selection and education of medical men for this duty, in a volume prepared in honor of one who, with all his versatility, is perhaps most eminent as a teacher and molder of ideals in the medical profession.

Change and adaptation to new conditions has been the lot of the doctor since medicine emerged from its enslavement to the doctrines of Galen, and the profession has had many more difficult adjustments to make than those involved in taking up the problems of the flying men; in fact, until the Great War gave such impetus to the development of aëronautics, very few of the profession at large had realized that there were any such problems. It is not remarkable, then, that at the beginning the assignment of medical officers to air service units was more or less fortuitous, nor that the characters most desirable in the squadron medical officer were arrived at empirically. Only the test of time brought out the peculiar importance and responsibility of the squadron doctor, and made apparent the differences between the successful and the mediocre, so that a type was defined by a process of gradual elimination.

At the first glance these men may seem to have little in common in their previous training and professional activities. One was in civil life an ophthalmologist, another an obstetrician, a third a country practitioner, the next a neurologist or a laboratory worker. In age they vary from twenty-five to nearly fifty, though it is less common

for the very young men to make good in this field. Let us, then, consider the factors, environmental and personal, which have brought about this development.

The basal unit of the Air Service is the Squadron, which is relatively small, but must be self-contained, as the exigencies of the service may require it to be very much isolated. The proportion of officers in this group is very large, much larger than in any other branch of the service. Again, the average age of the officers is very low; they are hardly more than boys, and still have many of the boy's characteristics. These young officers are engaged in a service fraught with many dangers other than those incurred in fighting, and with factors of isolation, personal responsibility, and strain, which are specially difficult for the very young. Furthermore these fliers are relatively highly paid, and they have been encouraged to consider themselves as a *corps d'élite*, set apart and different from the rest of the world. There yet remains from the earlier and more perilous days of aviation the idea that these are *enfants perdus*, who should be excused for living vividly while life is theirs. Women particularly seek them out and shower their favors upon them. Lastly, they have been given little disciplinary training, in deference to the highly technical character of the duty they perform. It is hardly strange, then, that, while these young men are essentially normal, they have none the less presented special problems for the medical man. We can make no adequate approach to the medical aspects of aviation without keeping in mind these factors and their physical and psychological bearing.

With these facts in mind it is easy to understand that the doctor with youth in his heart, tact, sympathy, insight, ability to live with and as the others without sacrificing their respect, frankness, courage, and a background of sport, has stood pre-eminent. Such traits have made of the medical officer the familiar friend and counselor, and it is to such men that these boys have come with their worries, physical, social, moral, or spiritual, and have not gone away uncomforted.

To reach the necessary degree of understanding and acquire the flier's respect, the aviation medical man must fly, at least as a passenger. Only in this way can he understand the air man's language and think his thoughts or enter into his experiences. In no other way

can the doctor learn what it means to loop, spin, dive, or make a landing. Without these experiences in common the doctor is kept at arm's length. In brief, the squadron medical officer's success is proportional to his humanness and practical psychology.

In order to measure up fully to his responsibilities, however, the doctor in the Air Service must have special training in applied physiology, somatic and psychic, for the laboratory has made great strides in the study of flying fitness, the causes and nature of flying stress and fatigue, the recognition of their early symptoms, and the measures for their prevention and treatment. The medical officer should be able to apply the simpler tests in the field, and to decide whether it is necessary to send the flier to a laboratory for more complete examination.

The aviation medical laboratory is an institute of applied physiology, which has already proved itself indispensable to the development of maximal efficiency in aeronautics. It has a threefold function—the routine application of special methods of examination to the individual flier in order to determine his fitness or the nature of any disability, the instruction of medical officers for field and laboratory service with the air forces, and the prosecution of researches into every phase of physiology, psychology, and medicine which may affect man's adaptation to life in the air.

In the medical organization of the air forces, then, we must provide for two groups of officers with rather different duties, the field officers or "Flight Surgeons" and the laboratory workers. The lines may not be too sharply drawn, however, as there should be every opportunity for the interchange of duties. Indeed, the laboratory examinations and the research into aviation problems can be carried on much better by men who have had some field experience as well, or at least have made flights as passengers.

It follows from the foregoing that the aviation medical service must be separated, at least so far as the personnel is concerned, from the other branches. For it is not economy to give the medical officer months of special technical training only to have him transferred to some service to which this training is inapplicable.

With regard to the future in peace times, it seems probable that there will be little difficulty in supplying the laboratories with staffs sufficient to carry on the work, because of the opportunities

for research. But the field surgeons present a rather different problem, as it is unlikely that the narrow prospects of an army medical career will attract the highly gifted man we desire. Perhaps this contingency could be met by limited periods of active service in a special reserve corps, and the offering of training in aviation medicine in our best-equipped medical schools. In countries where a form of national service prevails it should be relatively simple to have a reserve of trained doctors of the best type.

The development of civil and commercial aviation may create in time ample scope for an interesting professional branch. But whatever the difficulties to be surmounted as time goes on we must recognize now a sturdy neophyte in the Temple of Hippocrates, the "Flight Surgeon," at once a foster-son of Dædalus, a disciple of Leonardo, and a votary of St. Elias.

PERSONALITY AND DISEASE

By Frederic J. Farnell, M.D., Providence, R. I.

Psychiatrist to Providence Public Schools; Director of School Psychiatric Clinic; Neuro-Psychiatrist, Providence City Hospital; Sero-Pathologist, State Hospital for Mental Diseases; Consulting Psychiatrist, St. Joseph's Hospital and Sophia Little Home for Delinquent Girls, etc.

"SYNOPTIC man is one who sees the verities of life in their true relations, properly co-ordinated and subordinated, and who, in particular pursuits, however absorbing, does not ignore the unity of the whole, nor overlook the universal aspect of even the commonplaces of life."

I wish to express my great appreciation to the committee for the compliment they have given me in asking me to contribute to the Osler Anniversary Volume. In what I have to say I shall endeavor to study conciseness and brevity:

A French scientist once said, "In scientific research be extremely careful for fear you may find exactly what you are looking for." In the field of medicine such words could be no more true, either in behalf of the patient who may enumerate innumerable symptoms, or the physician who consciously or unconsciously observes only the apparent symptoms. How often the internist will base his complete diagnosis upon a complex of defensive or reactionary symptoms and avoid or even neglect the actual setting of those signs, especially so with regard to the interrelation or linking together of the systemic organs, either through the nervous system or through the vascular system, with its vast quantity of blood and its complex biochemical formulæ!

Except within the study of neuroses and psychoses the problem of individuality or makeup is rarely examined, and yet without it the full value of the organic or even functional disorder is far from complete. Self-preservation is man's uppermost wish, and hence his adaptative mechanism must meet fairly and squarely not only the preservation of its species, but also its social attributes and their environmental adjustment. It is here that motive and conduct

reaction, with either its corresponding instinctive demands or its emotional evaluation, largely is manifest, offering complex settings and transitory as well as variable symptom-complexes. Thus one may readily observe that oftentimes a far greater number of symptom indicators arise from origins that have no apparent direct relation to the organ involved, and develop in a region one may never suspect disturbed. It has always been the tendency to take man at his own valuation, and then to assume that the most sure way of finding out how such and such a symptom developed is simply to ask him, not recognizing the fact that defensive reactions are obstacles in way of a final interpretation as well as a recovery. These defensive reactions serve as excitants and irritants in the connecting chain of neuro-physical and neuro-psychical components, disturbing now the vegetative mechanism, again an emotional, still again the instinctive, adding many symptoms quite foreign to the initial disturbance, and often cloaking the actual difficulty. For example: a woman of forty years was treated for hemorrhages from the bowels, said to be due to sclerosis of her intestinal vessels. Sclerosis immediately roused an emotional activity, and environmental maladjustment arose. Her behavior towards this maladjustment naturally took on an apparent preservative coloring, whereas in reality her emotional factors and her instinctive demands in turn disturbed her vegetative system, with the result that cardiac, gastro-intestinal, and general vasomotor symptoms became quite obvious, destructive rather than preservative. Then, again, with total disregard of this growing neuro-psychophysical complex, she is quietly informed and courageously accepts from the internist the statement of "non-compensating chronic heart." (How close one still is to the initial vascular sclerosis.) All phenomena are now involved, body and mind, vegetative system, instinct, emotion, and personality. What a plight the family, as well as the patient, now face, for with each rise or fall in the threshold of feeling in the patient there was a corresponding modification in the emotional and instinctive life of the immediate family.

When approached, at this time, by the psychopathologist, who observed the entire problem from the standpoint of maladaptation towards self and environment, it was quite obvious that the initial hemorrhages were traumatic, from "marble" stools incident to

spastic constipation of autonomic origin. Hence one might infer that her autonomic system was "conditioned," and probably so determined by the fact that her makeup for years prior to her primary disorder was neuropathic (vagotonic). Conflicting, emotional trends broke down this "conditioned" system and added more cardio-vascular signs. They were, however, signs of vegetative disharmony, a loss of tone rather than a destruction of tone. A return to society was soon acquired by the breaking down of her emotional defenses, strengthening her instinctive demands and readjusting her vagus tone.

The complexity of this problem is far reaching and, at times, discouraging. In systemic disease processes of the spinal cord, where toxic substances or biochemical changes in the blood are utilized as indicators of the disease and its activity, due consideration should be given to the makeup of the individual, and his response to emotional stimuli and instinctive demands, before relegating some of his symptoms to the pigeonhole of imagination. It may not be a surmise to state that such toxines or biochemical phenomena as produce the cord lesion might produce a lesion in the ganglionated cord of the sympathetic chain, or it (the toxine) may so "condition" the autonomic system as to select the organic lesion. The personality factor, the behavioristic response, is quite manifest in syphilis of the nervous system, and interest should lie in not only striving for a cure, but so stabilizing the makeup as to lessen the possibilities of late syphilis manifesting itself in personality changes. For example: a man with a manic makeup developing meningo-encephalitis might, presumably, be grandiose in his psychic sphere. His readjustment should not only be remedial as far as his organic process is concerned, but also his "ego," his self, and his relation to society require adjustment. May there not be a close relation between the disease process (histopathological) and the personality with its behavioristic and emotional components (psychological) in such a case? But still more marked is the ever-present fear and those horrible anticipatory imaginings of the tabetic and his pains. Even after, treatment with subsidence of the actual neuritic pains, should a non-tabetic pain occur the pain-stimulus undoubtedly reproduces in kind and often in degree the original pain-stimulus. The emotional experiences and activities in these patients are alert, quick, and instantly

responsive, with the result that the fear probably influences the autonomic system.

There are patients, also, whose autonomic system not infrequently causes a phenomenon not unlike intermittent claudication. For example: a man of fifty, whose makeup was quick and active, whose emotion was swayed by the rise and fall of luck, and one whose sex life was never subjected to a normal control, develops at forty-three the tabetic syndrome. His remorse for a poorly spent sex life and his regret at not maintaining an economic grip upon himself led to depressive thoughts and later physical neglect. Examination not only revealed an organic disorder of the tabetic type, but also a distinct vegetative disturbance of the cardio-vascular type and a modified instinctive reaction with emotional instability. Environment might exaggerate one or all. Specific treatment caused the abatement of his organic subjective symptoms. Yet with this much under control he continued in morbid fear of the return of his pains, and whereas primarily the anxiety reaction accompanied the organic reaction, it was manifest alone. His autonomic difficulty was of the sympatheticotonic type, and treatment directed accordingly at the time adjusted that phase. There still remained the anxiety disturbance and his modified instinctive demands. Environmental adaptation in the latter, and a gradual eradication of his fear with the actual disappearance of his real pains and the creation of a dream-like memory of those true pains, the patient soon became quite comfortable and adjusted himself to society. It would appear that the patient's cardio-vascular system was "conditioned" through an autonomic sensitization, and that his emotional reaction was brought out not only by a stimulus which did not originally call it up, but also that a lingering emotion might have continued and produced recall even after the actual subsidence of true symptoms.

McDougall states that the idea of self and the self-regarding sentiment are essentially social products, that their development is effected by a constant interplay between personalities, between self and society, and its conception must be always of one's self in relation to other selves. That is, one must often give up pleasure-winning ways of satisfying one's self and adapt himself to any new condition arising. This self-sacrifice may bring about a conflict

between the pleasure-pain and reality motives, and in so doing return to the infantile, with a complete destruction of one's ideal, and maybe a progressive separation of his personality from the community in general. In the compulsion neuroses there is a regression of the sex craving to its earlier stage, with the development of an Œdipus mechanism.

One can but feel the great value of this mechanism as seen in many cases of so-called "chronic invalidism," especially true in the fifth and sixth decade in women. It usually manifests itself at the stage of menopause, and gradually becomes a fixed state of both mental and physical destruction. Since all love has as its fundamental object the preservation of species, either in self or through self, then that failure in one's eagerness to reach an ideal may not only warp the personality of the patient, but also destroy the personality of the child, and both the neurosis in the former and the psychosis in the latter will undoubtedly take on the Œdipus-incest complex with poor chance for readjustment. These patients frequently complain for years of vague and poorly recognized physical complaints which rather often symbolize unsatisfied cravings. For instance, one young man has tried all sorts of doctors, quacks, etc., to obtain a permanent removal of hair from his face. An absence of a secondary sex character would enhance his feminine characteristics and complete a more or less cloaked female conduct reaction. This young man was left at two years of age with his mother by the sudden death of the father. The mother brought him up under the most strict and yet good environment. They schooled together, read together, had the same interests in music, literature, and poetry. The boy became proficient in music, became an art and poetry critic, and worked well under guidance. When he reached the age of fifteen his mother, then forty-seven, had an accident, and evidently developed a "traumatic spine," with the result that she has grown less and less adaptable to herself or her environment. This physical incapacity upon the part of the mother caused the son to attach himself more strongly to his mother, and both gradually became crippled in such a way as to leave them inadequately equipped to deal with reality, the mother frequently enumerating what might have resulted "if" such and such a thing had not occurred, and her son might have been a "big chemist" or a "poet of the highest

order" if such a thing had not happened; the son in turn emphasizing trivial occurrences and indicating his regrets accordingly. At this time the mother is an invalid, with gastro-intestinal and urinary disturbance, the former manifest by spastic constipation and periodical diarrheas, and the latter by frequency (organic examination negative). The son has marked insomnia, indigestion, and "nervousness."

Presumably there is a distinct unconscious conflict related to success both in the mind of the mother and the son. Emancipation of the son has not taken place. The mother is incapable farther of idealizing in reality. Destruction of omnipotence in life and love is an admission of actual loss of species preservation. Truthfully to meet the reaction would mean a social insult of a severe type. To build a defense reaction means to separate one's self from his social life with the complete collapse of social values, and a substitution in both mental and physical symptoms of such psycho-sexual activities as conversion of the all-powerfulness of thought into autoerotic and incestuous symbols.

The extent to which investigations into personality and its relation to all disease process is of value can be reached only by making such an examination a part of the history of all patients. Many times patients are treated for "local" symptoms when their greatest difficulty is their makeup and its adjustment. Man is first of all a social animal, and the struggling desire for life's existence and for a rational fulfillment of it is becoming more and more a struggle between self from a psychological viewpoint and society from its social aspect, and from such he must be so considered and treated.

Bergson says, "When a shell bursts, the particular way it breaks is explained both by the explosive force of the powder it contains and by the resistance of the metal. So of the way life breaks into individuals and species. It depends, we think, on two series of causes, the resistance life meets from inert matter, and the explosive force, due to an unstable balance of tendencies which life bears within itself."

MEDICAL EXAMINATION OF MEN FOR MILITARY SERVICE: SOME OF ITS PROBLEMS, LESSONS AND RESULTS

By Sir James Galloway, K.B.E., C.B., M.D., LL.D. (Aberd.), F.R.C.S. (Eng.), F.R.C.P. (Lond.)

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In other circumstances it would have been the wish of the writer to contribute a paper giving the result of clinical observation, as an expression of regard to an acknowledged master of clinical medicine, but my old Chief well knows the urgent circumstances that for a period of time obliged me to relinquish my work as a clinician in order to undertake duties involving direction of, rather than personal participation in, medical practice.

I hope that the following account of some of the more directly medical aspects of the work done may not be devoid of interest.

Before the Great War the medical examination of recruits for the army was carried out by medical officers, retired or on the active list, and by civilian medical practitioners. The standard used was that laid down in Army Medical Service Regulations, and the men were passed as "fit" or "unfit." No attempt was made to place them in grades or categories. This system did not lend itself to accurate investigation and record of the physical condition of the men, and gave partial and misleading information as to the health and physical state of the population.

At the beginning of the war, when the first great voluntary rush to the colours was witnessed, the same system of recruiting was pursued, but under new and greatly increased difficulty, owing to urgent pressure of time and want of suitable accommodation for medical inspection.

On October 20, 1915, the scheme of recruiting associated with the name of Lord Derby came into operation and caused a further great flocking of recruits to the colours. The medical examination of these

men, which was carried out under great difficulties, caused so much unfavourable public criticism that the War Office made a complete change in the procedure of medical examination. Fortunately for the country, the medical administration of the War Department at home was then in the hands of Sir Alfred Keogh.

On December 24, 1915, the War Office ordered the formation of Medical Boards to replace the system of examination by single medical officials previously in practice. These boards were designed to consist of a president and three or four members. The examining members in many cases were civilians, but the president of the board was a military medical officer, usually holding the rank of Lieutenant-Colonel or Major. In a few cases these officers were still on the active list, but usually they had retired from the army before the war.

These boards were instructed to place the recruits in categories. The first Army Council Instruction dealing with this important matter was issued in January, 1916, and laid down the following categories of fitness:

1. For general service.
2. For field service at home.
3. For garrison service, (*a*) abroad, (*b*) at home.
4. For (*a*) labour (road making, entrenching work, etc.)
   For (*b*) sedentary work (clerks, etc.)

It was expected that each board should be able to examine 200 men daily.

It will be noted that even at this date the system of categorisation involved two conceptions: the first derived from purely medical data—the man's physical condition and state of health at the time of examination; the second involving administrative considerations, indicating the form of service for which he was presumed to be fitted on entering the army. The task of combining these two ideas was one of the main difficulties to be faced by the boards, most of whom were largely civilian in composition; this difficulty increased as time went on until in 1917 the attempt had to be abandoned. The attempt to solve the problem at one decision of the board gave rise to much confusion, and ultimately much unrest in the minds of the public—a trouble that was never satisfactorily dispelled.

In April, 1916, a classification certificate was issued for the

first time to men who had been medically examined. This document became of much importance in the recruiting system and developed ultimately into the grade card of the Ministry of National Service.

On May 19, 1916, Army Council Instruction 1023 was issued, which divided men into five categories:

(A) Fit for general service.
(B) Fit for service abroad.
(C) For service at home only.
(D) Temporarily unfit for service in A, B, C, but likely to become fit in six months, and meanwhile either
(E) Unfit for service in A, B, C, and not likely to become fit in six months; or awaiting discharge or reclassification.

Classes A, B, C, and D were further subdivided into three categories.

This Army Council Instruction was for use not only by Recruiting Medical Boards, but also by regimental officers and all others within the army. There were at least thirteen categories in which men could be placed. These details are given to show how completely classification to aid administrative requirements overshadowed classification on purely medical grounds.

During 1916 recruiting, which had now become compulsory for certain sections of the adult male population, was carried on more intensively, owing to the ever increasing demands for men. As an inevitable result, the recruiting machinery and methods came under public criticism. It is in the medical board and at the hands of the medical men working on these boards that the recruit first feels the actual touch of compulsory military service—his medical examination is his initiation into military methods. It is only to be expected, therefore, that the public will watch critically the methods employed by the boards and examining medical officers. The medical boards—their medical administration and organisation—had to bear the brunt of this criticism, much of it badly informed and far from helpful, much of it influenced by political prejudice. Later the administration of recruiting under the Military Service Acts was given over to a special department of the War Office and placed under the control of Brigadier-General, now Sir, Auckland Geddes.

At the end of 1916 it was found necessary to institute more close supervision of the medical boards with a view to reorganisa-

tion, and a special medical department was formed to undertake this work.

In December, 1916, and early in 1917, the writer inspected nearly every recruiting centre throughout the country in order to obtain information as to the methods used and the quality of the medical work. It was manifestly clear that as the war progressed recruiting would bear still more hardly on the population, interfering more and more with trades and occupations, until at length only the essential industries could be permitted to continue. With this prospect in view, it became necessary to arrange the medical machinery to be not only efficient, but to give as little offence as possible. The days of voluntary recruiting had passed; recruiting and medical examination now concerned every effective man in the community.

Reorganisation was brought about just in time, for on April 5, 1917, the Military Service (Review of Exceptions) Act came into operation. This Act provided for the calling up for medical examination of large numbers of men who had previously been excepted from the operation of the Military Service Acts. It will be remembered how difficult it was to put the provisions of this Act into operation and how in course of time the operation of the Act produced acute political disturbance. The intensity of feeling against the operation of the Act manifested itself largely by embittered criticism of the working of the medical organisation of the Recruiting Department of the army. After an anxious period marked by much disturbance, a Select Committee of the House of Commons was established to enquire into the administration of the Act, which made the following amongst other recommendations:

> "The Committee recommends that the whole organisation of Recruiting Medical Boards and of the medical examinations and re-examinations should be removed from the War Office and placed under civilian control."

In consequence of this recommendation Sir Auckland Geddes was appointed Minister of National Service, and the previously existing Department was thoroughly reconstituted. The Recruiting Department of the Adjutant-General's Office, including the Medical Section, was transferred to the Ministry of National Service, and henceforth recruiting for the army with all its medical organisation passed into what proved to be the last stage of development. After

a strenuous period of preparation the reconstituted Ministry of National Service commenced as from midnight, October 31, 1917.

During the year 1916 the experience gained of the work of recruiting medical boards under the army had been gradually collated, with the result that during this year the organisation, the personnel, and administrative methods of the boards underwent a gradual change. In the latter part of the summer the boards had gradually been placed on a new basis, so that when the great change took place from military to civilian administration, no noticeable jar to the machinery occurred. The organisation and administration proceeded on the methods which had been previously thought out, and which had now the opportunity of becoming fully developed.

It had become increasingly obvious that the attempt to superimpose a classification adapted to assist the administrative side of the army on work done by medical boards, now largely civilian, could not be continued, both for reasons of efficiency and on account of the social and political difficulties which such a method of classification inevitably brought in its train. The old army categories were guides to posting officers, based only partly on the result of medical examination. Classification of a man in one of the existing categories was therefore clearly the function of the army, and not of a board of a civilian ministry.

It was necessary for the new recruiting organisation to establish certain broad principles of classification of the men supplied to the army, for it would be useless to supply 1000 men fit only for employment as clerks when the demands of the army were for 1000 fighting men. Classification was therefore essential, but the medical and administrative aspects of the classification had to be sharply differentiated—relegated to civilian medical boards on the one hand, and to the military medical organisation within the army on the other.

Experience had shown that men of military age can be classified by medical examination into four great groups, determined by physical considerations alone:

1. Men free from serious defects or organic disease, of good muscular development, actual or potential, the movements of their joints unimpaired, their special senses acute, of good intelligence and at the time of being

handed over to the army, free from such infectious and contagious diseases as are not transient or rapidly curable.

2. Men fulfilling the above conditions, but whose special senses, e.g., eyesight—may be below the normal standard, but nevertheless sufficiently good for all ordinary purposes. Men in these two groups are capable of active service.

3. Men with defects which do not interfere with their vocation in civil life or with organic disease not likely to be incapacitating for a considerable period of years. These men must possess fair intelligence and be able to perform the duties allotted to them regularly. Men in this group are required to perform the multifarious auxiliary services required for a modern army.

4. Men whose defects or disabilities, physical or mental, are of such a nature or of so severe a degree as to render them unfit for service in the army.

It was on these considerations that the four well-known grades of the National Service Medical Boards were established, and from the time that the National Service Ministry undertook medical examination for recruiting the grading of men was carried out on the principles indicated.

During this period of reconstruction the actual organisation of the boards themselves had undergone changes. The fully developed National Service Medical Board consisted of a president and four members. The examination of the men was conducted on a sectional method. Experience had shown that the best results in medical examination from the point of view both of accuracy and of standard results were obtained if the candidate was examined by the members of the board in turn, each examiner in addition to a general view of the recruit paying attention especially to certain sections of the examination. The president of the board co-ordinated the work of the examiners, collated the results in every case, arranged for more formal consultation of examiners in difficult cases, and always pronounced the final grading of the recruit. The methods of the National Service Medical Boards are given fully in the instruction which was issued at the commencement of the work of the Ministry, the last edition of which was published in December, 1918 (M.N.S.R., 88).

The National Service Medical Boards, constituted on this basis and composed of the best available practitioners left in the country,

by degrees developed into a very efficient organisation for the estimation of physical fitness. The quality of their work naturally improved with time, and now the members of these boards, to the number of 3000 to 4000, have acquired special knowledge of methods of examination, of the conditions underlying physical fitness, and aptitude in the recognition of what makes a man fit or unfit which will be of great service to the State in the future. The work reacted beneficially on the profession itself; it brought medical colleagues together in all parts of the country; they worked together, and got to know each other well. The work developed in some respects in the nature of a post-graduate course of training. These good results were much appreciated and favourable opinions were expressed to the writer on many occasions.

To give an indication of the work done, it may be stated that from November, 1, 1917, to October 31, 1918, 2,425,184 medical examinations were carried out by the boards; in May the numbers reached 456,599, and in June, 475,416.

The Development of a Standard for Estimating the Fitness of Groups of Men. At an early stage of the work, before the boards developed their final phase, it became clear that there was an opportunity of obtaining an intimate knowledge of the health of the community, especially of the conditions producing deviations from the normal, degeneration, and disease, and particularly the effects of the habits and occupations of the people.

It soon became desirable to obtain an index of the condition of groups of the population as compared with what might be considered the normal standard. After some consideration, the following rough indication was arrived at, and has proved to be a serviceable guide.

The suggestion as to the method of obtaining such an index is due to Professor Arthur Keith, of the Royal College of Surgeons. Taking the results of the medical examination of 1000 young men who may fairly be considered to have been reared under good conditions, it was found that seven companies of 100 men should be in Grade I; two companies in Grade II; and of the remaining company of 100, three platoons of 25 in Grade III, and one platoon of 25 in Grade IV. In other words, 1000 young men drawn from a normally healthy section of the population should yield seven

companies of Grade I men; two companies of Grade II; three-fourths of a company of Grade III, and one-fourth of a company of Grade IV. Quoting Professor Keith's words in a very helpful letter addressed to the writer:

"We cannot get a better method of giving a concrete expression to the degree of fitness than that, yet the method is too clumsy for ready use. We need a more concise method of estimating and expressing the degree of fitness—a figure which will give us the relative degree of fitness in any batch of men examined by a medical board. The method I would propose is one used in anthropological work. Let us suppose the board has just examined 1000 men with the following result:

700 are placed in Grade I.
200 are placed in Grade II.
75 are placed in Grade III.
25 are placed in Grade IV.

Each Grade I man has his full unit of fitness.....	700	units
Each Grade II man we will assess at $\frac{3}{4}$, or 75 per cent of a unit. The 200 men have amongst them 200 x $\frac{3}{4}$....	150	units
Each Grade III man, assessed at $\frac{1}{2}$ unit, gives us 75 x $\frac{1}{2}$..	37.5	units
Each Grade IV man, assessed at $\frac{1}{4}$ unit, gives us 25 x $\frac{1}{4}$...	6.25	units
	893.75	

That is to say, in this artificial but yet approximately accurate method, the battalion of men just examined had 893.75 units of fitness—or cutting the expression short—the amount of fitness was 89.375 per cent of the total possible. The *index of fitness* of that group of men may be expressed as 89.3."

This index, which we speak of as "Keith's index," has been employed from time to time in our work, and has proved useful in forming an estimate of the relative value of man-power in different parts of the country and in different groups of the population.

For instance, the following table gives an idea of the quality of the men obtained for military service in a large section of the country, including populations occupied in agricultural pursuits, in mining, in the steel and iron trades, and in textile factories.

Example of Wide Divergence in Physique of Population in Neighbouring Areas. Extract from the report of a National Service visitor

TABLE I

This table shows the results of the medical examination of men between the ages of eighteen and twenty-five years, engaged in the staple occupation of the area in which they are shown. The basis for calculation was 1000 cases, but in one or two areas the number examined in the particular industry fell short of this number.

Area and Occupation	Grade I	Grade II	Grade III	Grade IV	Total	Index of Fitness	Keith's Index
1. Agriculture.	748 74·8%	130 13·0%	94 9·4%	28 2·8%	1000	898·75	89·875
2. Miners.	764 76·4%	94 9·4%	114 11·4%	28 2·8%	1000	898·5	89·85
3. Agriculture.	719 71·9%	155 15·5%	88 8·8%	38 3·8%	1000	888·75	88·875
4. Miners.	689 68·9%	151 15·1%	105 10·5%	55 5·5%	1000	868·35	86·835
5. Engineering trades.	609 60·9%	239 23·9%	134 13·4%	18 1·8%	1000	859·50	85·950
6. Agriculture.	620 62%	230 23%	116 11·6%	34 3·4%	1000	859·0	85·9
7. Iron and steel manufactures.	602 60·2%	256 25·6%	112 11·2%	30 3%	1000	857·5	85·75
8. Factory workers, woollen trade.	387 54·5%	78 10·9%	171 24%	74 10·4%	710	771·85	77·185
9. Factory workers, lace manufacture.	75 44·9%	45 26·9%	38 22·7%	9 5·3%	167	777·5	77·75
10. Factory workers, woollen manufacture.	375 37·5%	317 31·7%	270 27%	38 3·8%	1000	756·8	75·68
11. Factory workers, cloth and tailoring trade.	118 38·8%	75 21·4%	117 33·5%	39 11·1%	349	743·75	74·375

after visitation of Emergency Boards in a manufacturing area to enquire into the reason for the relatively high percentage of men placed in Grade III:

(A) Emergency Board, dealing with recruiting of colliers. April 5, 6, 8 and 9, 1918; 412 men examined and graded.

Grade I	II	III	IV
319	39	50	3
77.4%	9.4%	12.1%	.9%

(B) Emergency Board, dealing with the recruiting of colliers. April 5, 6, 8, and 9, 1918; 306 men examined and graded.

Grade I	II	III	IV
221	53	25	7
72%	17.3%	8.1%	2.2%

(C) Emergency Board, dealing with munition area reserved occupations and colliers. April 5, 6, 8, and 9, 1918; 314 men examined and graded.

Grade I	II	III	IV
257	27	29	1
81.8%	8.5%	9.2%	.3%

Combined average gradings of all Emergency Boards in this region dealing with this class of men, mainly colliers:

Grade I	II	III	IV
70.6%	12.4%	13.2%	3.4%

(D), (E) Emergency Boards dealt with cotton operatives, weavers and spinners, working in factories instead of colliers and munition area reserved occupations. The population examined was in a neighbouring portion of the country to the areas dealt with by Boards A, B, and C.

The visitor remarks:

"The difference is marked even in the waiting room, and becomes striking in the examination hall. Age for age the colliers strip much better than the cotton-mill operatives, and are as a class muscular and well developed. The difference is revealed in a more exact manner by the returns."

(D) Emergency Board. During March, 1918, 40.95 per cent of the men examined were placed in Grade III and 16.8 per cent in Grade IV; combined, 57.5 per cent. During April 5, 6, 8 and 9, 1918, 184 men were examined and graded and 106 postponed, as the Deputy Commissioner of Medical Services considered they would obviously fall within Grades III and IV.

The 184 examined and graded were distributed as follows:

Grade I	II	III	IV
57	64	56	7
30.9%	34.7%	30.1%	3.8%

If the 106 cases postponed, presumed to be Grades III or IV, are added, we get the following figures:

Grade I	II	III	IV
57	64	169	
19.6%	22%	58.2%	

The visitor records his opinion that the grading by the board was in general correct, and adds that the Deputy Commissioner of Medical Services is of opinion that work in the moist and overheated atmosphere of the cotton mills has a profound effect upon the physique and health of the operatives when extended over long periods, so that they age quickly.

(E) Emergency Board. During the month of March, 1918, the men examined by this board consisted almost entirely of cotton-mill operatives, and the returns show a daily average of 51.35 per cent of Grade III and 8.5 per cent of Grade IV. Daily combined average, 59.85 per cent.

On April 5, 6, 8 and 9, 1918, there was a considerable admixture of colliers—126 were examined and graded.

Grade I	II	III	IV
53	27	36	10
42%	21%	28.5%	7.9%

These figures, though eminently unsatisfactory when compared with the returns of a purely miner "comb-out," give a percentage of 36.4 per cent of Grade III and IV men, as compared with the 59.85 per cent of the cotton operatives in the previous month.

For purposes of comparison the following table is added:

TABLE II

	Grade I	Grade II	Grade III	Grade IV
Combined average gradings of boards examining mainly colliers in the region	70.6	12.4	13.2	3.4=16.6
Combined average grading of all men examined throughout a wide area of the country in April, 1918	55.9	19.8	19.2	5.1=24.3
Grading of 290 cotton operatives examined by Board D, on April 5th, 6th, 8th and 9th	19.6	22		58.2

A medical official in this area made the following commentary:

"The average man is an old man before he reaches the age of forty. . . . The folk of his part of the country are hardworking and industrious, and from an early age absorbed in industry; youths on being questioned frequently say they have no time for any games; they begin work young, work long hours, and too often think they are fully compensated if they make big wages. Thus the growing boy gets no chance of healthy outdoor exercise to develop his frame—he is too tired at the end of a hard day's work to trouble about physical culture. He is not troubled by his physical condition, he accepts it with dull contentment—after all he is only like his fellows. He works in a mill which has to be kept at a high temperature. He comes out in the evening weary, heated, and debilitated. The climate is damp and cold, he readily contracts rheumatic and bronchitic affections. Rheumatism affects his heart; hernia is easily produced when the muscles are poor and flabby, especially when there is frequent cough or when the work is really beyond his strength. Varix and flat foot are natural results of long hours of standing, when the muscles are flabby, anæmic, and weary."

Report upon Condition of 2994 Men between Forty-three and Fifty-one Years, Examined in Neighbouring Areas of Boards D and E. The following table is of interest, as it indicates the physical state of a number of the older men examined in areas in which the population is employed in work of practically the same nature as in the areas of Boards D and E. All these areas are in the same part of the country.

TABLE III

Diseased Conditions	Number	Per Cent
Varicose veins.	602	29·2
Heart affections.	462	15·5
Hernia.	374	12·5
Rheumatic affections.	315	10·5
Deformed toes.	308	10·3
Emphysema and bronchitis.	268	8·9
Varicocele.	234	7·8
Hæmorrhoids.	235	7·8
Deafness and otitis.	214	7·2
Flat feet.	172	5·8
Arterial degeneration.	124	4·2
No disability of any kind noted.		8

The preceding report throws light on the effect of occupation on the physique of a population inhabiting a well-defined section. The

reports that follow reflect the influence of race, environment, and occupation on the physique of a definite group. The statistics of the examination of aliens are derived from boards in London.

TABLE IV

CAUSES OF REJECTION AMONG ALIENS OF JEWISH RACE EXAMINED IN LONDON BETWEEN SEPTEMBER 20 AND NOVEMBER, 1917, WITH CORRESPONDING FIGURES FROM SCOTLAND.

RACE	NUMBER EXAMINED	REJECTED	PERCENTAGE REJECTED	PERCENTAGE REJECTED FOR PULMONARY TUBERCULOSIS
Russian Jews.	495	135	27·2	9·1 Add to the 135 rejected 23 relegated to the reserve, disability not stated, 158, or 32.1 per cent.
Scots.	10,000	440	4·4	1·1

Details of Causes of Rejection

Pulmonary tuberculosis	45
Valvular disease of the heart	17
Bronchitis	12
Trachoma	8
Disease not stated	7
Disordered action of the heart	5
Emphysema	4
Epilepsy	4
Poor physique	2
Defective vision	3
Mentally defective	3
Albuminuria	2
Duodenal ulcer	2
Varicose veins	2
Sycosis	1
Ascites	1
Curvature of spine	1
Nasal caries	1
Gunshot wound head and leg	1
Otorrhœa	1
Scar after appendicitis	1
Fracture right leg	1
Deafness	1
Chronic mediastinitis	1
Glaucoma	1
Disseminated sclerosis	1
Rheumatoid arthritis	1
Corneal nebula	1
Kyphosis	1
Withered right arm	1
Oto-sclerosis, incurable	1
Old choroiditis	1
Sciatica	1
	135
Relegated to reserve (disability not stated)	23
	158
Ages.	
Between 18–25	24
Between 26–30	30
Between 31–35	35
Between 36–41	46
	135

TABLE V

COMPARATIVE FREQUENCY OF COMMON DISABILITIES IN 1100 BRITISH AND 1370 ALIENS OF JEWISH RACE, LONDON

DISABILITY	PERCENTAGE AMONG BRITISH	PERCENTAGE AMONG RUSSIAN JEWS
Pulmonary tuberculosis.	2·1	19·2
Other diseases of lungs.	5·0	13·5
Eye diseases.	·7	7·9
Ear diseases.	3·2	7·3
Diseases of throat and nose.	2·1	6·6
Diseases of heart.	12·3	14·9
Mental diseases.	·4	·4
Gastric diseases.	2·1	4·4
Syphilis.	1·1	2·0
Gonorrhœa.	·6	2·0
Epilepsy.	·3	1·4
Obesity.	·9	5·3
5 feet 6 inches and under.	44·9	77·8
Defective feet.	12·2	24·7
Defective teeth.	22·8	21·0
Illiterates.	·2	37·1

TABLE VI

PERCENTAGE OF GRADING OF BRITISH YOUTHS OF EIGHTEEN AND ALIENS OF JEWISH RACE RESPECTIVELY, LONDON

GRADE	BRITISH	RUSSIAN JEWS
I	72·1	67·5
II	15·1	16·2
III	7·2	10·0
IV	2·5	3·8
Deferred	3·1	2·5

The Deputy Commissioner of Medical Services reports as follows on the above table:

"Two thousand British youths were examined and eighty Russian Jews of this age—no more appeared for examination at this date. They were all born in the Russian Ghettos, nearly all of German extraction, brought to England in early life and passed through our schools.

"On these figures their grading corresponds very closely to that of the British youths, and presents a very marked difference to that of adult Russian Jews; the inference appears to be that the Russian Jew deteriorates and becomes diseased chiefly during early manhood."

The above description and notes partly explain the way in which the work was done and give some indication of the results obtained.

The writer acknowledges the arduous service and good work of his colleagues and assistants.

For many years it has been the wish of those interested in social and racial progress to have a mass of information based on sufficiently accurate observations to estimate the physical condition of the people at the time, and to serve as a datum line from which progress or retrogression in the future could be judged. More than one effort has been made to study the problems influencing the health of the people, but have been fruitless because sufficiently accurate data have hitherto been wanting. There is now available much information giving many of the data required, some of which is now in the process of analysis and collation.

In addition to information concerning the men of military age, facts are being collected by degrees from various sources respecting the health of infants, children, young persons of school age, and women. The opportunity, therefore, is at hand for making an extensive medical survey of the population, but in order to make the foundations for future opinions complete and firm, arrangements must be made to obtain information comparable to that obtained respecting the adult population of military age during the past four years. The state of our manhood at the beginning of life's work should be under survey continuously, and at intervals thereafter the state of the population should be investigated. It is only by methods such as these that matters of such vital importance as the effects of occupation on our workers of all classes and the results of measures intended to improve the public health can be estimated. Without this information, plans for the improvement of our racial stock will be badly made and progress must be at random. The medical profession, now awakening to the sense of its responsibility for the health of the community and not merely for the ill-health of the individual, must obtain information of such importance. But the signs of the times indicate that now is the opportunity to secure what we require. Let us not forget the words of a very wise and friendly adviser:

> "Dimidium facti qui coepit habet; sapere aude:
> incipe: qui recte vivendi prorogat horam,
> rusticus exspectat dum defluat amnis: at ille
> labitur et labetur in omne volubilis ævum."

AMERICAN RED CROSS CHILD WELFARE WORK IN FRANCE

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I VENTURE to offer for this commemorative volume a brief account of the American Red Cross activities in behalf of French children during the latter part of the war period. I do this with some confidence, because Sir William Osler's great interest in all that pertains to child life is well known, and it was my privilege to hear this interest expressed when I reported to him in person at Oxford last July on the doings of the Children's Bureau. Moreover, it is becoming increasingly apparent that medical research cannot be confined to the laboratory or even to the ward, but must extend also to dealings with people in social groups, to the investigation of the causes of their common miseries and to the application of adequate methods of relief. Progress in these broader fields requires methods of research not unlike those of the clinic.

France during the latter months of the war offered a peculiarly promising field for child welfare work for the following reasons:

(1) The importance of better work for the children of the nation had been sounded throughout the land and was recognized by all intelligent citizens.

(2) The birth-rate of France, the lowest in Europe before the war, had sunk to less than half its usual figure—to about 8 per 1000—a reduction which, if continued, would of itself destroy the nation. It could be claimed, for example, that in comparison to America, every infant life in France was at least twice as valuable.

(3) France had already in operation many activities tending to reduce infant mortality and to foster child life. Methods that have been proven successful in England and America owed their origin to France, notably the Consultation de Nourissons, founded by Budin in 1892, and the Goutte de lait by Dufour two years later.

An older mutual benefit organization widespread in France is the Mutualité maternelle, with its many branches, which for a small sum of money assures to all members competent obstetrical service and an allocation permitting the mothers to rest for some weeks after confinement. This society is said to have lowered infant mortality 7 per cent.

(4) France has enacted two laws which have far-reaching possibilities in the protection of early childhood. By the Loi Roussel every child under two years confided to a woman other than its mother for its care becomes automatically under government supervision. It insists that factories employing women provide *chambres d'allaitement* for nursing mothers and *crèches* for older children. The Loi Strauss, passed just before the war, 1913–14, allows an allocation of one franc a day for the mother, one month before the birth of her child, and one and a half francs per day for four weeks afterwards if she remains home and cares for it.

Unfortunately the exigencies of the great conflict interfered greatly with the enforcement of these beneficent regulations.

In normal times about five thousand women in France are employed in factories; during the war, the number exceeded a million —at once a partial explanation of a low birth and a high infant mortality rate. These facts, briefly stated, indicate that the French nation was fully alive to the need of conserving its children and had led the world in devising methods to accomplish this end. With the war and the taxing of all the resources of the country for immediate measures of defense many of the activities on behalf of mothers, infants, and young children had to be curtailed or discontinued. Nearly all the nurses and physicians under fifty-five years were called for military service, and many civilian hospitals were turned over to the army or closed.

(5) America entered the war in April, 1917, and in the late summer of that year the Children's Bureau was organized under Dr. William Palmer Lucas as part of the Department of Civil Affairs, American Red Cross. The other bureaus working in the closest co-operation were the Bureau of Refugees, the Tuberculosis Bureau, and the Bureau of Reconstruction in the War Zone.

It will be recalled that that fall and winter and the following spring were very critical times for the allied arms. The balance of

military power after the defection of Russia seemed to favor Germany, and France was turning toward its sister republic across the sea to bring to her the additional assistance needed to rescue her from German greed.

It was during these anxious months before the fighting qualities of America's raw troops had been tested, or the extent of our military effort was fully appreciated, that aid was proffered by the American Red Cross for the civilian population of France.

(6) The whole population, official and unofficial, wealthy and poor, without regard to religious faith or social standing, accepted our offers of assistance for the children with the utmost gratitude and with every evidence of cordial co-operation.

(7) Through the generosity of the American people we had large means at our disposal, and a constantly increasing number of carefully selected physicians, nurses, and others familiar with the various phases of child welfare work.

These, then, were the outstanding elements in the unique situation: (*a*) A great country fully alive to the importance of increasing and preserving its child population, but with its means of carrying on its plans greatly curtailed because of a great war; (*b*) assistance extended to all classes of children in a sympathetic, tactful manner, from the large resources of an allied sister-republic. Such a combination of favorable circumstances may never occur again, and they offered such unusual opportunities to demonstrate certain methods of infant welfare that it may be worth while to place them on record.

The Children's Bureau arrived in France early in August, 1917, with a staff of about a dozen members. The number was increased by nearly every boat until 100 physicians, 200 nurses, and as many more nurses' aids and other assistants especially interested in child welfare, were in the service of the Bureau. The effort from the first was not to implant American methods upon the older country, but to assist it in working out its own problems.

It is not the intention of this paper to describe the work in any detail, but rather to mention briefly certain features of it which have general application both at home and abroad.

Rural Dispensaries. One of the first jobs the Bureau was asked to undertake was the medical supervision of a colony of 500 children

gathered at a large military barracks near Toul from villages which were subjected to gas attacks. After some months of patient effort this large group of children was made into a model colony. In connection with it was organized a dispensary and a hospital, first of a few, later of 200 beds, which ministered to the civil population for miles around. Soon it was learned that there were large manufacturing towns within reaching distance which were almost without medical service. With the support of the American Fund for French Wounded a dispensary service was established in perhaps a dozen of these centers. Rooms were secured in each through the kind offices of the officials, and twice a week at a specified hour, a physician, nurse, and one or more nurses' aids would arrive by an auto-ambulance and hold a clinic. Simple supplies were carried in the ambulance, which was used also to bring urgent cases to the hospital.

These ambulatory clinics were held at various other sections, both in France and Belgium, behind the fighting fronts. The automobile was always hailed with pleasure. The routes were known and often the doctor would be stopped and asked to see some special case along the way.

The value of this method of bringing medical aid to a rural population was abundantly proven. A similar system is applicable in many remote districts in other countries. Wherever the rural mail carriers go these dispensary units could visit, ministering to the sick and preaching the gospel of personal hygiene and child welfare. One automobile and staff could serve eight or ten different communities. In some towns a district nurse should remain in residence, spending her time in house-to-house visiting and in bringing patients to clinics.

The Detection of Contagious Disease at Evian. The reception, care, and distribution of the *repatriës* at Evian, returning to France after spending months in the hands of the enemy, was one of the most interesting and moving experiences of the war period. It is too well known to require more than a reference. To the Children's Bureau was allotted the task of detecting and treating infectious disease found among the 200 to 500 children passing through Evian in two convoys each day. A large hotel was converted into a 200-bed hospital, and with this and a number of detention wards and convalescent homes many acute and chronic infections were stopped

at the border and prevented from spreading disease throughout France. Perhaps no better opportunity has been afforded anywhere of studying communicable affections common in childhood.

In the admirable methods the French introduced for bathing, delousing, clothing, feeding, and transporting these unfortunate elderly derelicts and children to their new homes representatives of the Children's Bureau actively co-operated. Much information was obtained on the subject of child-placing in all its phases, in hospitals, asylums, colonies, and private homes, through our experience with the *repatrié* children.

Exhibits in Child Welfare. Exhibits as a method of propaganda are more familiar in America and England than in France. Two sorts of exhibits were arranged by the Children's Bureau in conjunction with the Rockefeller Commission against Tuberculosis, in which the subjects of Child Welfare and Tuberculosis were graphically depicted. The larger exhibits were held in several of the principal cities of France, beginning at Lyons. They were opened with the cordial approval and assistance of the officials and prominent citizens. The story was told by means of lectures by French physicians, by demonstrations of the exhibits many times each day, and by cinema, indoor and outdoor, to enormous crowds, and for the first time by a cleverly acted "Punch and Judy" show, the *guignol*, which was first introduced at Lyons, and was now used to show to delighted audiences of parents the bad results to the baby of indifference and neglect, and the happy consequences that follow its proper care. In glass booths real physical examinations of children were conducted; babies were weighed, bathed, and clothed. The value of nose and throat work was demonstrated on the patients and dental work actively carried on. The attendance at Lyons in three weeks was over 170,000, including nearly 50,000 school children, and as a result the number of patients at the welfare clinics in the city were doubled.

Other smaller exhibits were arranged for in several of the departments of the country. Approximately two months was spent in a department—about a week in each of its larger cities. Similar lectures and demonstrations, aided by lantern slides and cinema, told the story of the fight against tuberculosis and the healthful rearing of children. In each town where interest was aroused active

"follow up" work was planned and started, if possible, through existing organizations. Thus the enthusiasm stirred up by the American exhibits was continued under French auspices.

Courses in Nursing. It soon became evident in our work for children that house visiting on the part of a tactful nurse as we know her in America was rarely done, and that if our dispensary work both in small towns and large cities was to be really valuable, it should be supplemented by the instructive visits of nurses in the patients' homes. Fortunately many of our American nurses had been trained in Social Service, and were able to instruct the French pupil nurses in the field. Short courses in health visiting were begun in co-operation with the Rockefeller Commission and independently, designed to emphasize the simple rules of hygiene as applied to child welfare and to tuberculosis, and to lay especial stress on social service in the home. Active assistance was given by French physicians, who delivered the lectures and conducted the quizzes of the carefully prepared course. Practical work for the pupil nurses was obtained at the hospitals and dispensaries. These courses were given at Paris, Lyons, Marseilles, and elsewhere. They attracted earnest women—who, as they completed their training, were sent to assist the trained nurses on the field.

Those who are familiar with the great value of home visiting as a part of the medical work in America will join in the hope that this little demonstration in France will lead to its general introduction in connection with every hospital and dispensary.

Supervised Play. We were fortunate in having in the Bureau the services of a number of playground workers and recreational experts. It was possible, therefore, in connection with all our exhibits and in the various colonies and institutions under our charge, to give practical instruction and demonstrations of the value of supervised play in physical, mental, and moral training. In the games such qualities as initiative, self-reliance, pluck, team-play, and so forth, were stressed. The children quickly learned the games, and it is expected that many French children who loved to romp when shown how and to whom this kind of play was novel will not forget it when the Americans have gone home.

Intensive Infant Welfare Work. What would happen if every baby in a limited community received proper care? We had unusual

opportunity to begin the answer to this question in a number of places because of the co-operation of French officials, who placed at our disposal the accurate statistical information of the district. A ward in Paris and several other limited areas in town and country were selected. Each day the names and addresses of the babies born in these areas were sent to the Red Cross representatives. These infants were immediately visited and, with the aid of French agencies, adequately helped if there was need. That is, it was made financially possible for the mother to remain home and nurse and care for her baby, and she was encouraged to so do. She received instruction both at her home and at a nearby welfare station. Each case was studied individually, and the treatment required to "save the baby" by its own mother, administered. Thus each dependent baby in the district was given more of an equal chance with the baby of the well to do.

A society was organized in the 14th Arrondissement, Paris, under the patronage of Maire Ferdinand Brunot, "Patronage Franco-American de la première Enfance," to begin this intensive work there. Through this means it was hoped greatly to reduce infant mortality in that crowded district and to demonstrate that babies can be saved if those care sufficiently who know and have. We are confident that this "100 per cent work" for which this Patronage Society stands is a distinct forward step in Infant Welfare Work, and that time will demonstrate that the plan is practical and that this method born in Paris as a war measure may prove a model applicable in other times and places.

Co-ordination of Child Welfare Work. With the well-known imagination and impulsiveness of the French people and their fondness for children it is not difficult to understand that there are in France many kinds of organizations and societies devoted to child care. Not a small part of the labor of the Bureau was to help the most deserving and to co-ordinate the activities of those dealing with similar problems.

Many grants made by the Red Cross to children's societies and institutions reduced in their resources because of the war were conditional upon the introduction of some suggested improvement in plant or method. It seemed in many instances that this merging of interests could be secured only through American suggestion,

but when once brought about will be continued in the future. In Marseilles and Lyons, for example, practically all the children's organizations were brought for the first time into cordial affiliation.

Such were a few of the more instructive attempts made by the American Red Cross to come to the aid of French children in the hour of their need. The occasion was unusual. In the process France became in a sense a voluntary laboratory for the testing of many phases of child care. It was possible, therefore, not only to bring assistance to the present generation of children of this gifted and industrious nation, but perhaps also to indicate some methods by which child life may become more healthful and happy in other countries as well.

MILITARY MORALE

By Edward L. Munson,

Brigadier General, General Staff; Colonel, Medical Corps, U. S. A.

WHILE the above subject is one not directly related to the practice of medicine, it still is not wholly dissociated therefrom, as it not infrequently pertains to group states of mind quite as abnormal and irrational as those which, in the individual, come to the attention of the alienist. Further, it may have a certain medical interest from the fact that, so far as the United States were concerned, the proposal for the institution of morale work, its successful experimental application, and its organization as a military agency, were all carried out by a member of the Medical Department.

One of the many blunders made by Germany during the war in its psychological estimate of other peoples was in deciding that the United States could not put forward a disciplined army of a fighting quality equal to the best that the Central Powers were able to present. To-day this mistake is conceded in Berlin, for it was American aggressiveness, quite as much as actual or potential force, that broke the heart of German resistance and showed the enemy not only that he could not win, but that stalemate tactics would not be tolerated and that he was sure to lose.

The morale of the American soldier was perhaps one of the most impressive things pertaining to his part in the war. The triple chain of confidence, cheerfulness, and willingness to suffer any sacrifice, so bound the troops together as to make them unbeatable. They knew it all the time—it did not take long for the Germans to find it out. The latter had spent generations in developing their armies to such a degree of efficiency that their organization was proclaimed to be the best ever upbuilt. Probably so it was, from the mechanical aspect; but it lacked in animating spirit to have full fighting strength. From their first contact with American troops, from Château

Thierry to Sedan, the flower of militaristic Germany was swept back, foot by foot, yard by yard, and mile by mile, until only the armistice saved retreat from becoming rout. These things were done by men who, called from the farm and bench, became in a few months an army of courageous, confident, self-sacrificing soldiers, whose presence the enemy feared and detested.

The sudden and stupendous expansion of an army to represent the might of an unprepared nation caused the full force of the War Department to concentrate at first on the problems of mobilization, organization, and procurement of material. With these preparations the spirit of patriotism was quickened.

It was felt, however, that morale, which with training is the basis of discipline, was so fundamentally important a matter that its growth should not be matter of chance. Napoleon had said, "In war, the moral is to the physical as three is to one," and all writers had recognized that good morale was prerequisite to military success. But the question of how to influence morale directly was largely unattacked.

In January, 1917, the writer, in an editorial entitled "The Soul of an Army," said: "There must be systematized education and training in the psychology of the soldier and of the war. This field is not now covered. It is a 'No Man's Land' into which neither line nor staff penetrate." Again on March 2, 1918, in a memorandum entitled, "Need for the Systematized Psychological Stimulation of Troops in the Promotion of Fighting Efficiency," he further urged the importance of the matter on the General Staff, with a result that a series of conferences was held on the subject by representatives of various organizations having to do with the prosecution of the war. In the meantime, the writer had been transferred to Camp Greenleaf, Georgia, and as Commanding Officer there tried out in actual field work, on a camp of some 35,000 men, the ideas advanced in theory. As a result of these conferences, and the successful demonstration of the practical value of the work at Camp Greenleaf, the General Staff decided to authorize the work and place it on a sound basis throughout the Army.

Accordingly, the following order was issued by the War Department:

"1. There is hereby created a Morale Branch within the General Staff. . . .

"2. The general functions of the Morale Branch relate to the improvement of the efficiency of the soldier through the betterment of morale.

"3. The Morale Branch shall have cognizance and control of the following:

"(*a*) The initiation and administration of plans and measures to stimulate and maintain the morale of troops.

"(*b*) The organization, training, co-ordination and direction of all agencies, military and civil, operating within military zones, in so far as they serve to stimulate and maintain morale in the army.

"(*c*) Co-operation with any morale agencies of the General Staffs of Allied countries in connection with military morale.

"(*d*) The supervision, co-ordination and direction of activities in the various departments, corps, and bureaus of the army for stimulating morale within organizations or among producers of munitions.

"(*e*) The supervision, co-ordination and utilization, so far as may properly be accomplished by military authority, of all recognized civilian agencies which might contribute, directly or indirectly, to the enhancement of morale. To this end, close relations will be established, through the Third Assistant Secretary of War as Director of Civilian Relations, by the Morale Branch, with all officially recognized agencies for the improvement of morale in the Army or Nation. It will not give official recognition to unrecognized voluntary agencies, though treating them with respect and consideration."

The writer was made Chief of the new Branch, which,with its military organization, including a number of various experts, as psychologists, sociologists, newspaper men, artists and cartoonists, advertising men, linguists, and others, at once set about the systematic stimulation of military morale.

It is not practicable at this time to go into details as to how this was accomplished, and is being accomplished; for the task is still uncompleted, and it is obvious that work of this sort is best accomplished as unobtrusively as possible. Disclosure of methods and purposes would arouse unconscious resistance and render far less plastic the human material which must be handled. Suffice it to say that exact methods were worked out in relation to the psychological forces which render them as relatively controllable and intelligently directed as the similarly unseen forces of electricity or

radium, and which will later be given out when such may be done without detriment to military purposes. An organization, sensitive down to the private in the company, was created whereby the morale agencies could function to the lowest unit. By it, favorable states of mind were induced and undesirable acts averted by processes more or less analogous to the elimination of infectious disease and the prevention of epidemics.

Morale work has its purposes quite as much in peace as in war. In the latter, patriotic purpose, mutual protection, and other factors tend to hold men together. But the signing of the armistice, and relief from the military tension along the above lines, released a horde of pent-up emotions which created most difficult administrative problems. These states of mind it was the duty of the Morale Branch to handle. Perhaps it may claim a certain efficiency in this respect, since nearly two million men have, at this writing, been demobilized and returned to civil life without the slightest disorder, where riots and disturbances against authority have repeatedly occurred in the troops of other nations during the same period. Also the men have been absorbed back into civil life in a good frame of mind toward the Government and Army, untainted by political heresies.

There are many qualities expressive of military morale. Some pertain to fighting only—others are stepping stones to that end. Discipline implies both training and morale. Training gives ability to fight, while morale is desire to fight. Both are necessary to victory. Morale is to an army what temper is to the Damascus blade, a "fighting edge" with a resiliency no shock can crack. If morale is as important as this, it is important enough to make every effort to cultivate it, and it thrives under such culture.

But morale is not merely enthusiasm or mental courage or the fighting spirit. It is all these, and more. It has a sterner element. It is that mental hardening which, in a body of troops, continues to function after everything else has broken. It is a quality which at the last desperate moment continues to function after all the conditions which have created it have disappeared. It is not only the will to win, but the refusal to consider anything else as possible. Military morale accordingly is mental fitness of troops for the work of war. It is to the mind what "condition" is to the body; good morale is

good mental "condition," bad morale is bad mental condition. The state of good morale must be relatively lasting, for the test of good morale is time and adversity.

In an army of a democratic government the soldier fights well only for ideals. Money or material reward is no inducement to the American soldier to face the bullets of the Argonne, but he seeks out death, with a smile on his lips, as the champion of ideals. He must know the reasons and principles of the cause for which he fights; and besides knowing, he must believe in them.

The morale of the army of democracy, therefore, must rest solidly upon the basis of conviction. If the soldier does not possess this on entering the army—and all do not—it must be given to him. Ideals are an essential part of his equipment. It follows, therefore, that information and education, the mainstay of democracy in peace, must be its strength in war.

There is such a thing as morale based on sordid motives, but its nature is comparatively temporary, and its quality is inferior. Such was the German morale, founded on a desire and expectation to take possession by force of the material things of this world. It was the same morale that held together the buccaneers and freebooters of all ages. But it could be successful only in material success. Hence the extraordinary spectacle of the powerful German armies, everywhere fighting in enemy territory and successful according to the map, falling apart without cohesiveness when definitively balked of their prey and finding their booty of the past snatched from them. They had no other ideals than those of materialism to sustain and inspire them. When these failed, morale was lost.

To these, the Allies opposed the imponderables. Their ideals of right, truth, honor, justice, and liberty shone more brightly after four years of adversity and became more precious as they were threatened. The thin Allied line might give ground under the mighty blows of the war engine; it might bend and stretch, but it never broke, because of the flaming spirit of the ideal that made death better than submission.

The Germans bolstered up their men with falsehood, as by the same way they sought to undermine the fighting spirit of their foes. They could be successful only so long as their deceit and falsehood were not found out. When this happened, they lost confidence in

their cause, their leaders, and themselves. America, through its morale methods, fights lies with truth. Its cause is just. It knows that against an unholy cause "the truth is mighty and will prevail." It knows that what it does in making a better soldier will make him later a better citizen. Its ideals are such as stimulate its men to victory and confound its foes. And right ideals win. Even such a crass materialist as Bismarck said, "It is the imponderables which weigh the most."

PHASES OF WAR SURGERY. EXTENSIVE, HIGHLY DISFIGURING WOUNDS OF THE FACE

By Charles A. Powers, M.D., Denver, Colo.

Professor Emeritus of Surgery in the University of Colorado.
Formerly Major, M. C., U. S. Army

THE incidence of high-explosive casualties in the present war has occasioned wounds hitherto unknown. Of these, the severely disfiguring injuries of the face are of marked importance. The carrying away of the lower part of the face may be immediately fatal (hemorrhage, shock, closure of the glottis), or fatality may result later through sepsis, secondary hemorrhage, pneumonia. In a given percentage of cases, however, the wounded soldier survives, only too often to be repulsive through his disfigurement, the reduction of which to the greatest possible degree has furnished the surgeon with difficult and perplexing problems, problems enlisting his sympathy as well as his skill. Not only should the soldier be made to present as comely an appearance as possible, but he should be able (wounds of the lower part of the face) to masticate well and to speak intelligibly. In gaining the best results, the surgeon must have the intelligent co-operation of the dentist; fragments of bone must be appropriately held by splints, dentures must be carefully made and applied. This co-operation between surgeon and dentist has found in this war application previously unknown.

The subjoined history and photographs are presented without further comment.

Case. P. C., aged forty-one years, single. Regt. Adjutant 3me Mixt. Zouaves. Serial No. 4441. Wounded by fragments of shell while in action May 18, 1916. Admitted to the American Ambulance Hospital of Paris, Ward 178, May 30, 1916.

Examination. Compound, comminuted fractures of the anterior, lower portions of both superior maxillæ, of both palate bones, of the vomer and of the anterior portion of the inferior maxilla. Much loss of

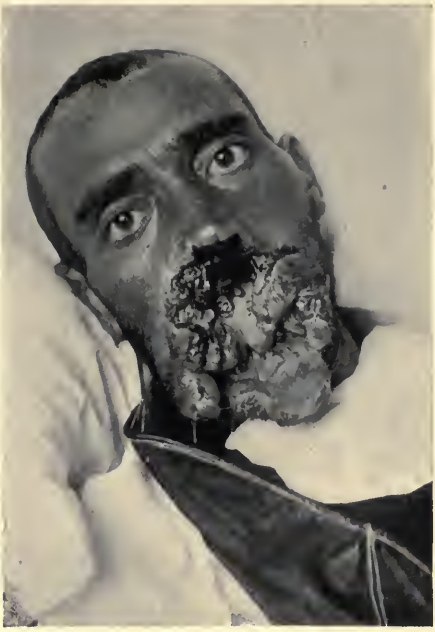


FIG. 1. CONDITION ON ADMISSION, MAY 30, 1916.

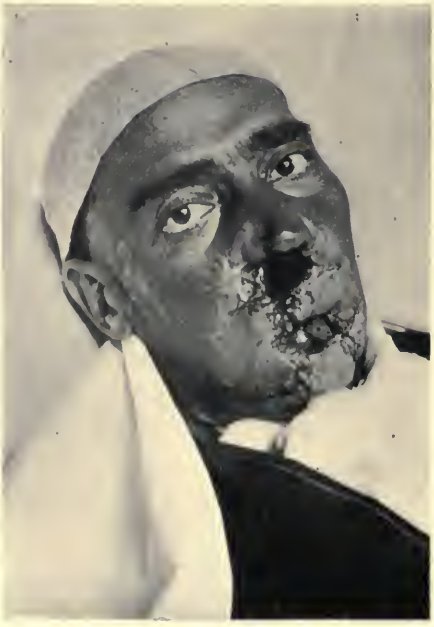


FIG. 2. APPROXIMATION OF UPPER LIP AND CHIN, JUNE 6, 1916.

FIG. 3. JULY 10, 1916, UPPER LIP FORMED.

FIG. 4. AUGUST 29, 1916, FORMATION OF LOWER LIP AND MOUTH.

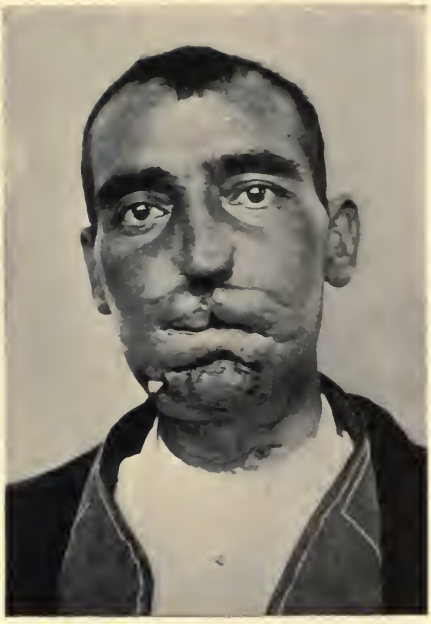


FIG. 5. SEPTEMBER 2, 1916.

FIG. 6. APRIL 11, 1917.

FIG. 7. CONDITION ON DISCHARGE, MAY 2, 1917.

bone substance, loss of all teeth excepting some upper and lower molars. Severe laceration and much loss of substance (considerable loss of mucous membrane) of the soft tissues of the face, especially those of upper lip, lower lip, and chin. Severe lacerations, with considerable loss of substance, of the tongue. All wounds septic and foul. Moderate fever. (Facial condition on admission shown in Fig. 1.)

Treatment. Hourly irrigations with permanganate solution, 1–8000, suitable tube feeding, attention to bowels, removal of *éclats d'obus* (local anesthesia), from front of neck; sitting posture. (The patient, a very intelligent professional soldier, co-operates with the surgeon and nurses in every way.)

Three days after admission, June 2, 1916, under local anesthesia, the fragments of the upper lip and those of the soft tissues of the chin were loosely brought together by sutures of silk-worm gut and horsehair. (Fig. 2, picture taken June 6, 1916.) (Note. June 10 the patient is up and about, doing well. Slight suppurative fever.)

July 3, 1916. The upper lip drops (Note: I am of the thought that an attempt should have been made to elevate this at the time of the operation of June 2, despite the severely septic condition of the wound.—C. A. P.), and under local anesthesia both sides of the upper lip and the adjacent portions of the wound are dissected free, lifted, and held up by large, stay, suture-guys, these suture-guys running to the soft parts over the anterior portions of the malar bones. (Guy scars shown in Fig. 3.) In addition, the right side of the lower lip is dissected loose from the tissues to which it had become adherent and brought up toward the upper lip, being held in place by sutures. Tissues of chin loosened and approximated as far as possible.

Note: July 7. Left side of lower lip loosened and held up by stay-sutures.

July 10. These latter procedures have been successful. (Fig. 3, photograph taken this day.) Note, July 20: The opening in the face is contracting rapidly.

July 31. Ether. Further plastic approximation of tissues. Necrosed bone removed from right side of inferior maxilla. (Small, loose fragments have been taken from all fractured bones from time to time.)

August 19, 1916. Operation, ether. Complete freeing of all tissues of the face, extensive freeing of tissues of chin well down on neck. Section of the cheek on right side at angle of present mouth. Mucous membrane brought to skin. Preliminary attempt at formation of lower lip. Chin tissues brought up and fastened to lower lip.

August 26. Further plastic operation. Right cheek slit out about 1¼

inches. Mucous-skin approximation. Right angle of mouth formed. Left cheek slit out about ¾ inch. Remains of lower lip brought over from right side and fastened to tissues of left side, thus forming a lower lip. Chin tissues undermined and brought up. (Fig. 4, taken August 29, 1916, shows formation of mouth and lower lip.)

Fig. 5, September 2, 1916, shows the result of this procedure; at this time (September 2d) the patient has not yet complete control of the saliva.

Small, additional plastic operations were done on September 17th, October 9, and October 31.

The patient spent the winter of 1916–17 in an annex hospital at Clichy awaiting further plastic procedures.

April 16, 1917. Ordinary Nélaton operation for the relief of the hare-lip shown in Fig. 5 (September 2, 1916) and Fig. 6 (April 11, 1917). In this last picture the smoothing out of the depressed scars and the return of a molded facial contour may be noted. At this time the patient is able to control the flow of saliva.

May 10, 1917. The hare-lip has been satisfactorily corrected (Fig. 7). The patient retains saliva well. There is firm, bony union in the fractured mandible. The dental department (Dr. Darcissac) has provided the patient with cleverly made, practically useful and excellent appearing artificial teeth. He controls saliva perfectly. Small operations have freed an adherent tongue. He speaks and eats well and presents the quite comely appearance shown in Fig. 7. (Photograph May 2, 1917.) His general health has been excellent since a month after his injury.

May 25, 1917. Patient discharged.

July 4, 1917. The patient writes me (C. A. P.) of a recently and happily contracted marriage.

Continued observation of a fairly large series of somewhat similar cases serves to impress upon me the advantage of complete military control of the given patient (fortunately these cases are exceedingly rare outside of the casualties of battle), the importance of deliberate and careful daily inspection, as well as the retention of the patient in a single hospital and continued attention by a single surgeon. Continuity of service, not often possible in war surgery, makes for the best results. It seems trite to say that the earlier skilled attention is afforded these distressing cases, the better will be the results.

A PSYCHOTIC EPISODE IN ROMAN HISTORY

A STUDY OF THE ABNORMAL PSYCHOLOGY OF NATIONS

By Charles L. Dana

I AM calling attention to a short period of human history between 50 B. C. and 44 B. C., during which time there was an extraordinary upset in human affairs—the world changed hands.

I wish to show that the phenomena of that period, as exhibited by certain national events, resemble a psychotic episode in the human individual. The analogy is not altogether fanciful, and is perhaps of more than academic interest; for it seems to me that it is suggestive of a new line of study—that of the abnormal psychology of races considered as units. The study is a difficult one, and what I present may be nothing more than suggestive, but I feel satisfied that it is worth while, for such studies may help us in interpreting and forecasting national events and progress.

In studying the career of an individual for psychological purposes, we try to learn the make-up of his character, to get at his personality, to find out the amount and quality and proportions of his mental endowments. Some persons are simply defective quantitatively—they lack the mind stuff, they are imbecile or childish in intelligence; others are lacking in some single form of endowment, such as emotion, self-control, power of decision, or of initiative, being otherwise perhaps brilliantly intelligent. These are said to have a constitutional psychopathic inferiority. Others have an abnormal make-up, with overdevelopment of anti-social instincts; they form the criminals, the perverts, the eccentric and abnormal types. They are said to have a psychopathic personality.

In the life history of a normal individual, the ordinary methodical working of his thoughts, emotions, or behavior may become seriously disordered. Then we say he has a psychosis or mental sickness. This morbid mental condition may be slight and episodal, or it may be

persistent and lead to the loss of his health, property, personal responsibility, and death.

The history of a race or nation may be studied, just as we study the career of an individual. We may study its behavior for the purpose of determining its normality, or to find whether there is anything in the racial make-up that is comparable to a psychosis, or an inferiority, or psychopathic personality, or a quantitative mental defect. This is in line with the present trend, viz., that of studying behavior as well as that of applying the results of introspection, for the purpose of determining the condition of the mind.

As we consider the history of nations, I think we can recall instances in which there have occurred some things characteristic of the psychoses.

It is easy, for example, to conceive of a national exhaustion psychosis. This would be characterized by a general clouding and confusion, by indecision, by hallucination, lack of insight or foresight, and a general collapse of capacity to care for the person or its possessions. We may be seeing such things at the present time. There was certainly a psychotic confusion in Germany after the break-up of Charlemagne's empire in the ninth century. After three or four hundred years of futile wrangling and fighting, the only result was the establishment of 276 feeble independent states.

There are races which may, through partial deterioration, show a constitutional psychic inferiority—like the present race of the Persians, and that of certain Nyro republics. Perhaps the history of Korea illustrates this also.

Some nations seem to have what is equivalent to a psychopathic personality, i.e., they are abnormal in certain lines of their developmental activities. This was perhaps true of the Phœnicians, whose civilization was characterized by ambition to gain money, and who contributed nothing to the progress of the world in the domain of science, art, letters, or of mechanical or agricultural invention during the whole of their history.

A quality of constitutional inferiority may be said to characterize the Turks—"a race," says John Fiske, "politically unteachable and intellectually incurious, which has contributed absolutely nothing to the common weal of mankind."

There are races which belong to the high grades of feeble-minded-

ness. These races may show some intelligence, but they have not enough to enable them to exist nationally, except as dependents. A primitive and undeveloped race, however, may not be a feeble-minded one, for the test of intelligence lies in the power of living with some degree of order and happiness through its own exertions, like the North American Indians and Esquimaux.

The emotional state is the most unstable of the elements of mental life, the most easily affected by the strains and tragedies of life, and the most easily communicated to masses. All nations are more or less subject to emotional outbursts, to contagious obsessions, to illusions or misinterpretations of data. When these things pass beyond what the average intelligence and education of the people should correct, they come within the group of morbid mental states. The emotional attitude of the Greeks was characterized by obsessive passion for local and personal liberty, not for a large community welfare. This led to their undoing. The French had in 1870 an attack of episodal pithiatism, developed out of the exhaustion and suffering of previous years. They are said now by a German writer to have a "Gallic psychopathy" characterized by a passion for revenge!

It is too soon to characterize the development and spread of Bolshevism, but it is some form of racial or national psychosis; a great national movement based on the results of deprivation and suffering and stimulated by delusions—as we believe—or by misinterpretations of the laws of sound national development.

Thus I am sure it is safe to say that races, whether living under the common arrangements of organized government or not, are quite proper objects of studies in abnormal psychology. Such study may help to explain the rise and fall of nations and civilizations.

Historians have in the past attempted to describe the cause of the decline of individual races and civilizations, but their explanations have generally been based upon certain incidental conditions, such as an excessive amount of war, the conditions of the soil, devastations made by famine, epidemics, etc. These conditions all did exist, but they persisted in a measure because of the defects in the organization and mental qualities of the race. One-sixth of Italy s uninhabitable on account of malarial conditions, yet these could be removed if the people and its government wished, i. e., if it had the mentality to initiate reform.

Mr. Flinders Petrie, in his "Revolutions of Civilization," has contended that civilization is an intermittent phenomenon, that the civilization of certain dynasties of Egypt went through periods of development and decline, and that the same process took place in Europe. He puts the civilization which began in the fifth century B.C., and ended in the Age of Constantine, as a seventh period of European evolution.

Professor Petrie does not attempt to explain these recurrent phenomena, however, nor has anyone, so far as I know, attempted it in any general way. The suggestion that it may be due to the faulty make-up in the mentality of races is at least worth considering. We know that, given a certain personality, if it is subject to depressing or irritant conditions, it develops a special psychosis corresponding to the mechanism of the individual's character. So, when a nation or race is made up on a certain pattern, it will react to exhausting or depressing stimuli, in accordance with its mental mechanisms.

Let us now see what was the "make-up" of the Roman race.

The members of this race were certainly not constitutionally inferior or psychopathic. They developed, expanded, and controlled the destinies of the world for a thousand years. But, like many normal individuals who live lives of aggression and domination, they had some psychopathic and perilous periods, due to their natural characteristics.

The Romans started as a race of fighting farmers, and at the beginning, waged war mainly on the defensive. In order to retain their homes and land, they developed the sturdy virtues of discipline, valor, and obedience. They were only fairly intelligent, but they believed that they had superior qualities and were extremely confident of themselves. They were not strongly individualistic like the Greeks, but were willing to make personal sacrifice for the sake of the whole group.

They had an unimaginative state religion, and they prayed for their families and crops. They were not a sensitive people, not generous in spirit, were poor in emotion, with no great social gifts. They had little ingenuity, and until later developed no art or science—except those of war and farming.

Says Mr. Jerome in "Roman Memories," referring to the early Romans:

"The Romans were a people relatively deficient in sentiment and imagination; intellectually, they were not above mediocrity; they were self-confident, avaricious, severe, and pitiless, but were not needlessly cruel; they were remarkably free from envy, hatred, and malice; they had a strong feeling for gravity and decorum, and possessed to a degree higher than in the case of other ancient peoples the sentiment of justice.

"They had common sense, but no great mental nimbleness, nor clarity of vision. They were conservative, credulous, opportunist, formalist. These qualities were joined to their defective imagination and insight. Their strongest characteristic was their volitional power; they were iron-willed, energetic, determined, patient, and self-controlled. Their leaders were not afraid to lead, and the masses were not impatient of restraint, not disinclined to obey nor backward in facing death or pain."

Says Smith in "History of Rome":

"We may trace the superiority of the Romans, first to the strength and firmness of their character, which endowed them with confidence in themselves, still more with confidence in one another; to the power of command over themselves and not less of command over others; to the mutual sympathy and brotherly feeling nurtured by the perils they had encountered and the triumphs they had won together, and to a consciousness of natural fitness to rule and an imperial destiny to accomplish. The vaunted patriotism of the Romans, which was undoubtedly both sincere and active, may be resolved into a sense of dependence upon one another and an independence of all besides, which taught them to regard their city as the center of their universe."

The Romans prospered. As they became more experienced and realized the resources and enjoyments of a larger life, they secured, through their primitive virtues, their intelligence and practical training, the things that art and greater social development in other countries could furnish. They bought art and culture and good living. They found it easier to plunder than build, so they became predatory in habit, and war was used to enrich their homes with everything that the world could furnish.

They could not fight and plunder and keep their acquisitions without retaining their discipline and all that went to make successful warriors. As they had continually to fight not only to acquire wealth, but to defend themselves against other robbers, they were led to become efficient in constructing roads, fortresses, and buildings.

They retained their pride and egotism, which showed itself in an intense desire to dominate and to fear any form of personal or national enslavement.

For about 250 years, under the Kings, the Roman people were busy organizing themselves and establishing their city, pursuing agriculture, and defending themselves against their neighbors. Then the republic began, and with it the beginnings of the Great Addiction. Rome began to expand; it felt the desire for power, and this gave it plunder, a great commerce, and riches. It conquered Sicily, parts of Spain, and all of Italy. At about the same time it destroyed Carthage and conquered Greece, and by 165 B. C. became master of the whole Mediterranean basin. Later this people completed the conquest of Africa, Sulla, Marius, and Brutus plundered the East and Spain, while Cæsar plundered Gaul. When the latter was assassinated he was planning to conquer the Parthians and pay the debts of the Romans. The desire for power and territory and money grew, as does the desire for opium. The more they possessed, the more they needed to defend what they possessed. At first this was an ambition of the people or nation, a group ambition, but later it became an individual ambition. It was specialized, and the leaders or the classes sought power and riches for themselves. This led to civil wars: the wars of the Gracchi, of Sylla and Marius, the wiping out of the Samnites, and the control of all Italy.

The nation was on the point of falling to pieces through the debts and exhaustion of the state, the rivalry and ambitions of the leaders, and the neglect and incapacity of its administration.

Here is the Roman experience from 264 B. C. to 48 B. C.

War by Hannibal, first Punic War, 264–241 B. C.; second Punic War, 218–201 B. C.; conquest of Greece, 200–195 B. C.; conquest of Syria, Spain, and Cisalpine Gaul, 191–178 B. C.; Macedonian War, 168 B. C.; final conquest of Greece, 148 B. C.; destruction of Carthage, 146 B. C.; civil wars led by the Gracchi, 133 and 121 B. C.

Defensive and offensive war against the Teutons and Jugurtha, 110–101 B. C.; social war led by Marius, 90–86 B.C.; foreign and civil war conducted by Sulla, 86 to 82 B. C.; Gallic wars by Cæsar, 57 to 48 B. C.; conquest of the East by Brutus.

The condition of Rome at this period is summed up by Fowler somewhat as follows: There had been a sudden increase in wealth

which was misused and misspent, so that the nation was overwhelmed with debt. There was an abnormal increase of badly used slave labor; city life, greatly developed, was not wisely handled; wholesome family life had decayed; there was a decadence of women and of the old forms of state religion; the methods of education were wrong, and there had occurred an increase of disease, due to malaria in the country, to bad sanitary conditions in the city.

In Appian's "Roman History," Book II, Sect. 19, we are told that the Commonwealth had for a long time been disorderly and unmanageable. The magistrates were chosen by means of money and factional fights. Bribery and corruption prevailed in the most scandalous manner. The people went bought to the elections. The Consuls could not lead armies or command in war, because they were shut out by the Triumvirate. The Republic went without Consuls for eight months. Good men would not take the task. Finally mob violence broke out and Pompey was made Dictator, but his reforms were short-lived. A devotion to personal or clique ambitions had taken the place of loyalty to the government and love of the fatherland. The condition has been characterized as the beginning of national degeneracy and decline. But the work of Rome in the next three centuries disproves this.

It was rather a psychotic episode, precipitated by the weakening effect of wars, and excited finally by the enormous opportunities for personal self-indulgence, so that those things which should have gone to enrich and develop the state went to demoralize and confuse the people.

When addiction overwhelms an individual, there result mental confusion, delirium, clouding of consciousness, and a definite toxic exhaustive psychosis, calling for the offices of a physician or custodian.

It so happens that we have a picture of the times at this period, as accurate and vivid as if it were a product of the best kind of modern daily journalism. This is in the letters of Cicero, covering the period 50 to 47 B. C., in which latter year Cæsar crossed the Rubicon and later conquered Pompey at Pharsalia.

Cicero pictures the situation as hopeless if Cæsar wins. Historians agree that it would have been hopeless if he had not.

The letters show Cicero's views on the instability of the Republic,

the power of one general, the weakness of another. His letters portray the general distrust of those in authority and a despair for the future of the state and himself. I quote especially his references to Cæsar, as showing how keenly he feared another social war and civil disaster. All that he apprehended did occur for a time, but after Augustus had finished his proscriptions and restored social order, the state revived and grew in strength and efficiency for several hundred years.

In the year 50 B. C. Cicero had just finished his government of Cilicia, and he was on his way home, when he first got news of Cæsar's demands—viz., to be retained as governor of Gaul, and later to be elected consul. The Senate soon voted that if Cæsar did not resign he would be declared a public enemy.

Thereupon Cæsar crossed the Rubicon (49 B. C.), and civil war between him and the loyalists, led by Pompey, began. Pompey left Rome, fled to Brundusium, the southern seaport of Italy, and thence crossed to Epirus. Cæsar seized the government at Rome, garrisoned Italy, went to Spain, conquered the loyalists there; returned to Italy; then in January, 48 B. C., he crossed to Epirus, and in August, 48 B. C., won a victory over Pompey at Pharsalia. The Roman republic was ended.

Cæsar began—and Augustus completed—the medical treatment of Rome, bringing back the authority of Rome and its patriotism and passion for domination, to the government, and not to groups of individuals.

Specialization of power, without co-operation and authoritative organization, fails in national life as it does in personal life. This is the lesson drawn from the story of the Great Addiction.

[Many letters are omitted in order to shorten this article, such as give the picture of Rome when Catiline nearly succeeded, and tell the stories of the lives of the men of that time, Dolabella, Cœlius, Curio, Antony, Clodius, Milo. There were only two real men at this period—Cato and Cæsar.]

51 B. C.

Marcus Cœlius to Cicero:

With respect to our present divisions, I foresee that the senate, together with the whole order of judges, will declare in favor of Pompey: and that all of those of desperate fortunes, or who are obnoxious to the laws, will

list themselves under the banners of Cæsar. As to their armies, I am persuaded there will be a great inequality. But I hope we shall have time enough to consider the strength of their respective forces, and to declare ourselves accordingly. . . . In the name of all the gods, my dear Cicero, hasten hither to enjoy the diverting spectacle of Appius sitting in judgment on extravagance, and Drusus on debauchery! It is a sight, believe me, well worth your expedition.

Marcus Cælius to Cicero: 51 B. C.

Meanwhile, we are in the humor here of acquitting all criminals: nothing, in truth, so base or so villainous can be perpetrated that is not sure of escaping punishment. You will perceive how wondrously active our consuls are in their office, when I tell you that they have not yet been able to procure a single decree of the senate, except one for appointing the Latin festivals. Even our friend Curio has not hitherto acted with any spirit in his tribunate; as, indeed, it is impossible to describe the general indolence that has seized us. If it were not for my contests with the vintners and the surveyors of the public aqueducts all Rome would appear in a profound lethargy.

Cicero to Marcus Cælius: 51 B. C.

You mentioned something of a lethargic inactivity that had seized the republic. I rejoiced, no doubt, to hear that you were in a state of such profound tranquillity, as well as that our spirited friend was so much infected with this general indolence as not to be in a humor of disturbing it. But the last paragraph of your letter, which was written, I observed, with your own hand, changed the scene, and somewhat, indeed, discomposed me. Is Curio really, then, become a convert to Cæsar? But, extraordinary as this event may appear to others, believe me, it is agreeable to what I always suspected. Good gods! how do I long to laugh with you at the ridiculous farce which is acting in your part of the world!

ATHENS, October 16, 50 B. C.

Cicero to Atticus, Greeting:

If you have at last received my letter you will know that I have yours through our friend Acastus, and that I am in good spirits (*bono animo*) because Acastus told me of your improved health. But I shivered myself (*coborruisse autem me*) at your news of Cæsar's legions. . . . For myself, I seem to foresee a terrific struggle (*tantam dimicationem*) unless the same god who saved us in the Parthian war take pity on the state—even so, such a terrific struggle as there never has been before.

Cicero to Atticus, Greeting: FORMIÆ, Dec. 5, 49 B. C.

I have really no news, but it soothes me to write to you and to read your letters. (*Acquiesco enim et scribens ad te et legens tua.*)

My fears about the republic are very great. I have no consolation except the thought that if fortune bestows on Cæsar the supreme power he will not be so mad as to misuse his advantages. If he begins to run amuck my fears are more than I dare to write. (*Quodsi ruere coeperit, ne ego multa timeo quæ non audeo scribere.*) But whoever conquers there will come many evils and no doubt a tyrant.

FORMIÆ, March 8, 49 B.C.

What a difficult and calamitous business! (*Quem difficultem planeque perditam.*) How can Cæsar keep from a destructive policy? It is forbidden by his character, his previous career, the nature of his present enterprise and his associates. For what a following he has, what damned souls! what an abandoned and desperate cause! I foresee a massacre if he conquers, an attack on the wealth of nations, repudiation of obligations, recall of exiles, high office for the basest men and a tyranny intolerable.

Please introduce Terentia to the bankers; and send me news of Tiro, as you have done.

BRUNDUSIUM, Nov. 26, 50 B. C.

I arrived at Brundusium Nov. 24th. Terentia, who met me in the forum, told me that your second attack of quartan had passed . . . I hope that by your prudence and temperance your health has been restored. I have all your letters, each more delightful than the last. . . .

Cato has treated me shamefully and spitefully. He gave me a high character (which I did not want) but denied me a triumph, for which I asked, and how Cæsar exults over this wrong done me by Cato! . . .

I long to answer all your letters; though there is one to which I have no answer to make, and that is the one dealing with the perils of the republic. I am very much upset (*valde eram perturbatus*). What would you have me do?

From Letter to Tiro.

A. U. 704, 49 B. C.

But an invincible rage for war had unaccountably seized not only the enemies, but even those who are esteemed the friends, of the commonwealth: and it was in vain I remonstrated, that nothing was more to be dreaded than a civil war. Cæsar, in the mean time, unmindful of his former character and honors, and driven, it should seem, by a sort of frenzy, has taken possession of Ariminum, Pisaurum, Ancona, and Arretum.

From Letter XII, To Servius Sulpicius.

A. U. C. 704, 49 B. C.

The flames of war, you see, have spread themselves throughout the whole Roman dominions, and all the world has taken up arms under our respective chiefs. Rome, in the mean time, destitute of all rule or magistracy, of all justice or control, is wretchedly abandoned to the dreadful inroads of rapine and devastation. In this general anarchy and confusion, I know not what to expect; I scarcely know even what to wish. . . .

From Letter XIV, Cicero to Marcus Cœlius.

A. U. C. 704, 49 B.C.

The truth of it is, there is no calamity so severe to which we are not all of us, it should seem, in this universal anarchy and confusion, equally and unavoidably exposed. But if I could have averted this dreadful storm from the republic at the expense of my own private and domestic enjoyments, even of those, my friend, which you so emphatically recommend to my care, I should most willingly have made the sacrifice.

THE SCHEMATIC DRAWING OF THE EYE IN ITS HISTORIC DEVELOPMENT

(FIFTEENTH AND SIXTEENTH CENTURIES)

By Mortimer Frank, S.B., M.D., Chicago, Ill.[1]

THE difficulties encountered in examining an eye anatomically in earlier times probably led every auditor to form his own conception of that which was orally presented to him. These concepts naturally must have been very different, and so drawings were made for teaching purposes, some of which have been preserved. These have been carefully studied by Sudhoff.

Sudhoff's investigations commence with an anonymous *Anatomia oculi* on the back page of a thirteenth century MS. in the Sloane collection of the British Museum (420). The eyeball and its tunics are shown as made up of circles and divided perpendicularly by two straight lines into an anterior (left) and a posterior (right) half. Below the figure, at the left, appears *pars oculi exterior;* at the right, *pars oculi interior.* The innermost circle, which is not divided, is inscribed *humor cristallinus,* and the inscriptions from within outward in the hemispheres surrounding this are for the anterior half (*pars exterior*) as follows: *tunica aranea, humor albugineus, tunica vuea* (uvea), *tunica cornea,* and *tunica coniunctiva.* The *tunica coniunctiva* has been drawn like a perioscopic lens which gradually thins out towards the poles of the eyeball, an idea which probably originated from a misunderstood drawing of the cornea. The posterior half is inscribed, reading from within outward, as follows: *humor vitreus, retbina, secundina, tunica sclirotica.* From the upper and lower folds of the eyeball two straight lines lead to the right (*pars posterior*) and intersect at an acute angle (the limits of the orbit?) and at their point of intersection is written, *Hic tanget cerebrum;* that is, the place of entering the brain. From the equator of the posterior half to the point of intersection of the two straight lines is the inscription, *Nervus opticus,* without any linear limitation.

[1] Dr. Mortimer Frank died suddenly April 21, 1919, in his forty-fourth year, at his residence, 1059 Hyde Park Boulevard, Chicago, Ill.

In another Sloane MS. (981), belonging to the second half of the fourteenth century, there is a short text with an illustration pertaining to ophthalmic anatomy. The figure represents a cross-section of the entire head, in the center of which is an eye surrounded by circles and semicircles, like the coats of an onion. Here, as in the diagram above, the circles are divided by a perpendicular line into an anterior and posterior part, with the same inscriptions as in the foregoing. Behind the posterior part is a moon-shaped sector marked *Cerebrum*, surrounded by three semicircular segments inscribed with the names of the coverings of the brain.

The Vatican Library at Rome possesses the Codex Urbinus (246), a MS. written in the second half of the fourteenth century or the beginning of the fifteenth, including among its contents the anatomy of Mundinus. Where the structure of the eye is discussed, a later owner drew, on the margin of the page, a diagram of the arrangement of the coats of the eye in the manner already described and with the same inscriptions within the circles.

Chronologically following the preceding pictures is one in the Codex Leipzig (1183) ascribed to the first half of the fifteenth century. Sudhoff does not agree with Hirschberg of Berlin that this diagram should be ascribed to the Spanish-Arabian ophthalmologist Alcoati. This hasty pen and ink sketch of the fifteenth century upon the margin of a page was copied from some unknown source. The evidence is proof of the fact that, independent of Arabic tradition, a cross-section of the eyeball must have been handed down during the Middle Ages through the Occident. He also points out that the placing of the cornea outside the conjunctiva is directly contrary to Alcoati. Alcoati did nothing original in ophthalmology and surely not in his anatomy. The latter originated with the Greeks and from them passed to the Arabs and thence to the Occident, and to Salerno and other medical schools through many different channels, and finally also through the Latin translations from the Arabs. The Arabs made no anatomic investigations of their own on the eye, just as they made none on any other parts of the body. The many religious restrictions made the publication of drawings representing parts of the human body absolutely impossible or highly difficult. But even as other diagrams and sketches of organs were made in Alexandria, so there can be no doubt whatever that diagrammatic

drawings of the structure of the eye were made there and found their way during the Middle Ages to the Orient and Occident. On the other hand, we have no proof that all the pictures of the eye which are found in the Latin editions of Arabic authors come from Arabic tradition. Sudhoff does not doubt that the Arabs possessed Greek diagrams of the eye in graphic form, but no MS. of any Arabic work during the Islamic zenith contains a drawing of the eye.

During the second half of the thirteenth century, the decline of Islam, the Syrian Halifa wrote a treatise on ophthalmology of which two MSS. are known. The drawing in the Constantinople MS. (924) of the sixteenth century illustrates the structure of the eye and its connection, by means of the chiasm, with the brain. This picture, published several times without text by Hirschberg, dates from the Halifa MS. of the year 1560.

Another interesting drawing of the eye, which also shows a horizontal cross-section divided into an anterior and posterior portion by a median line, as in the Occidental models, is found in an Arabic MS. (3008) in the Bibliothèque Nationale at Paris, written in 1714. This is a very late transmission if we consider that the portion on the eye by the Syrian, Salah-Ad-din, is said to have been written about the year 1296. The drawing was first published by Pansier and later again by Hirschberg, but without the anatomic text which Sudhoff gives. It illustrates the combination of two cross-sections of the globe perpendicular to one another, and plays even to-day a certain rôle in the Arabic world according to Hirschberg. Sudhoff does not agree with Hirschberg's interpretation of the picture, which is of no consequence in this discussion. Whether it was the original illustration for Salah-Ad-din's text book, and as such inserted about the year 1296, or whether it was drawn without any influence from the Alexandrian or even Byzantine sources, Sudhoff is not prepared to say.

Further researches might establish for these graphic representations of the structure of the eye an earlier date than the year 1300, beyond which none of the present illustrations go. Earlier drawings by Hobeisch of the ninth century and by Hammar of the eleventh century have not been preserved, as far as recent researches have gone. The assumption might also be made that all these drawings found their models in a late Alexandrian period, which remained

alive in the traditions of the Orient and Occident far into the fifteenth century, if not longer, and which appear to have been not without influence even upon Leonardo and Vesalius.

The oldest printed illustration of the structure of the eye is found in the "Margarita Philosophica" by Gregor Reisch, published by Kaspar Schott at Strasburg on April 17, 1504. The external view of the eye on the same page is a revised reproduction by Johannes Peyligk and Magnus Hundt. The Freiburg Carthusian monk, Sudhoff says, undoubtedly got his drawing from tradition, as with most of the other illustrations in his book.

With this early accessible model created in the various editions of the "Margarita Philosophica," it found a place in other works, as, for instance, Hieronymus Brunschwig's "Distilierbuch." Very soon afterward it is found in many ophthalmic treatises, with alterations and additions. Independent modifications, however, are first observed in a rather similar illustration which Walther Reiff uses in his "Anatomie" (1541). However incomplete the illustration still is, there already appears a trace of some independent anatomic observation, some real study of nature. Reiff's picture of the eye had a long life and was reproduced by Anton Novarinus as late as 1681.

Individual conception does not come to the surface until the publication of the "Fabrica humani corporis" by Andreas Vesalius in 1543. His drawing is not wholly true to nature, especially as regards the crystalline lens. Vesalius could not free himself from the tradition that the crystalline lens had its seat in the center of the eye, a fact which he particularly illustrates in several detailed drawings.

In some respects it must be admitted that before this, through his own individual observations, Leonardo da Vinci had come nearer the truth than any of his predecessors or his successors up to the time of Vesalius. He not only treats of the anatomy of the eye, but also considers it from the viewpoint of optics.

George Bartisch, in his treatise of 1583, employs a schematic representation of the eye made up of seven superimposed plates, a common device of the fugitive anatomical pictures of the period. From this it was only a step to the models in three dimensions which sprang up in the seventeenth and were common in the eighteenth century. These were again abandoned for the actual eyes of dead animals, still employed in the teaching of to-day.

PHYSICIANS' LETTERS

By Fielding H. Garrison, M.D., Washington, D. C.

ONE of the earliest modes of conveying medical information known to physicians was by means of letters, personal or professional. These, in a much later period, were destined to be the originals of our medical periodicals and transactions. From the existence of two pediatric epistles from the physician Arad-Nanâ to the Assyrian king Assurbanipal (884-860 B.C.) on eye trouble and epistaxis in the little prince, his son, one might almost venture to infer the possibility of clinical correspondence between physicians themselves, as in the old medieval *Consilia* (consultations by letter). Morgagni's "De sedibus," 1761, is, of course, the most remarkable medical treatise in which the *consilium* is consciously used as a norm or mode of expression. From the days of Gentile da Foligno and Montagnana, it is a far cry to the huge interchange of letters between Bretonneau and his pupils Trousseau and Velpeau, the last and latest specimens of *consilia*. With the letters of Gui Patin (1601–72), things take a new turn. They are a vast gossip-shop and school-for-scandal, replete with the anecdotage and *médisance* usually associated with our profession. As we approach our own period, with its mania for smartness and efficiency, its multiplicity of labor-saving devices and its corresponding lack of large leisure for anybody, physicians' letters become dryer and more businesslike, with only a touch, here and there, of the Pepysian quality. Delightful exceptions are the Billroth letters, mainly rhapsodies about music. Only passing reference can be made to the various collections of Tissot, Frank, Scarpa, Jenner, Astley Cooper, von Baer, Pirogoff, Korsakoff, and others. The life and letters of Weir Mitchell will be a stately biography, which awaits its author.

Almost every biography of recent date is eked out by means of letters. Those of John S. Billings are a fair example of the modern tendency. His youthful letters, especially those from Civil War battlefields, are spirited and colorful; in the later period, they are

the plain business statements of one who has acquired the outlook of Stendhal's ideal philosopher—to see things as they are, with the clear, cold vision of a banker.[1]

In the earlier days of the Surgeon General's Library, Billings began to gather from his own extensive correspondence a small library collection of autograph letters of notable physicians. This collection has been very materially enlarged by liberal and valuable donations from Dr. A. Jacobi, Sir Lauder Brunton, and others. Brunton began his correspondence with the writer in the following letter, which may be embalmed in this keepsake as affording an interesting view of Huxley's ultimate attitude towards religion.

"May 5, 1915.

"I have been reading with great delight the charming memoir you have written of my dear old friend Dr. John Shaw Billings. I trust you will forgive me if I write to you in regard to a mistake you have made in what you say regarding another dear friend of mine, the late Thomas Henry Huxley. At page 373 you say on the questions of religion and immortality of the soul, Huxley's attitude was antagonistic. I knew Huxley very well, indeed, and for a long time spent my Sunday evenings generally at his house in Marlborough Road, where he and Mrs. Huxley had a 'high tea' every Sunday night, to which they welcomed any of their friends who might drop in without any formal invitation. I had been brought up in one of the straitest sects of Scotch Presbyterianism, and the Bible being the most interesting of the four or five books which I was permitted to read on the Sabbath, I naturally learned to know it well—so well indeed that I have only met two men in my life who, I thought, knew it better than I did, and one of these was Thomas Henry Huxley. Some of his opponents objected to his use of Biblical phraseology, but he used it simply because he was so steeped in the language of the Bible that he could not help it. But it was not the language of the Bible only that Huxley knew. He had assimilated its teachings and guided his life by them. Huxley has always appeared to me as one of the most religious men I have ever met. He was pugnacious by nature and detested Pharisees intensely, but I do not think that in all his writings you will find such strong language about them as that in the Gospel of Matthew, Chap. xxiii, 13, 14 and 15.

[1] Pour être bon philosophe, il faut être sec, clair, sans illusion. Un banquier qui a fait fortune a une partie du caractère requis pour faire des découvertes en philosophie, c'est à dire pour voir clair dans ce qui est."—Stendhal.

"In 1879 I married a daughter of the late archdeacon of Meath. Shortly after our return from our honeymoon we went together to Huxley's one Sunday night. He took my wife a little apart and began to ask her about herself. When she told him that she was a clergyman's daughter he asked about me. When she said, 'Dr. Brunton is a Presbyterian' he drew himself up involuntarily and said—not without some pride, my wife thought—'*We* were all Church of England people.'

"His natural turn for argument was fostered by his father, who set all his boys two and two at a time to argue a question. At the end of half an hour they had to change sides and demolish the view they had at first taken as best they could. When I tell you farther that after his death Mrs. Huxley told me that he had been buried at his own special request with the full Church of England service, I think you will agree with me that his attitude regarding the questions of religion and the immortality of the soul cannot properly be described as 'antagonistic.'

"Believe me,

"Faithfully yours,

"LAUDER BRUNTON."

Toward the end of his life, Brunton began to send to the Surgeon General's Library many gifts of unique value, among them his choice collection of autograph letters of notable physicians. These were accompanied by extensive commentaries, written out by himself. A few paragraphs, of historical and biographical interest, are worth quoting:

" September 27, 1915.

". . . I am sending you a batch of autographs: some are interesting, others are of no particular interest.

"You have probably a very large number of Acland's letters in the correspondence he had with Billings, because they were very fond of each other, but the one that I send you is interesting because Acland has put in it very shortly the dream of his life to make Oxford a University for the advancement of learning rather than for its dissemination. For a good many years I examined in Materia Medica in Oxford and during the period of examination I was always his guest. On one occasion a curious incident occurred which showed that Acland possessed to a very extraordinary degree indeed the power of foreseeing other people's intentions. It almost outdid any of Sherlock Holmes' adventures. I was going to the examination one hot afternoon and I must have been drowsy. I looked out at Oxford Station but did not see the name, and on the contrary saw in very large characters the name of Reading, which I afterwards found out belonged

to an advertisement of Reading Ales. I did not get out but at the next station looked up and saw that I had passed Oxford and got on to Banbury. I knew the students would all be waiting for me and I was much perturbed. I found that the only way of getting back to Oxford was to wait for two hours, which of course was far too long, or else to take a special train back. I at once got a special train and on arriving at Oxford Station on the up platform, to my astonishment, I found Sir Henry Acland waiting for me. I asked him how this came about. He said, 'I knew you had left London, for if you had not you would have sent a telegram. I knew you had passed Oxford, because you did not get out. I knew you would find out your mistake and take a special train back and here you are.' He said, 'I told the boys that you had been detained and I kept them. They are all waiting in the Examination Hall.' We went back to the Examination Hall, the examination began about half an hour late but otherwise as if nothing had happened. The special train, however, consumed almost the whole of my salary as examiner for the year at Oxford. . . . Heidenhain's letter refers to certain statements made by Lawson Tait. He said that Harvey had not discovered the circulation of the blood by means of vivisection. Harvey himself said that he had but Harvey was dead and could not contradict Lawson Tait; but Lawson Tait went on quite unnecessarily to say that this had been admitted in their evidence by Sir Henry Acland and Dr. Lauder Brunton. Both these men were alive and promptly contradicted Lawson Tait's statement. He searched the evidence but in vain, for the statements attributed to Acland and Brunton were not there. He then said that his informant was Mr. Jesse, secretary of the Anti-vivisection Society. Mr. Jesse said that he had done nothing of the kind, and Lawson Tait was left in the lurch. If Lawson Tait had been content to limit his statements to Harvey he would have been all right, but his memory played him false in regard to Acland and me. Lawson Tait was not at all a deliberate liar: he simply did not know what truth was. He could not distinguish between the products of his own imagination and objective facts. He was a student of medicine in Edinburgh University when I began to study. He still remained a student when I left, and as far as University was concerned he was never anything but a student because he could not pass the examinations. When he went up for examinations he gave what he believed to be the correct answer to the questions, but unfortunately these answers were not what the examiners wanted. They told him to go back and study for several months more. Finally he succeeded in getting a license from the College of Surgeons, but he never got a University degree. But the same excessive, lively imagination which was such an enemy to him at examinations befriended

him most thoroughly in debating societies. At the Royal Medical Society of which I was a member there was, on one occasion, a special discussion in regard to tracheotomy. Some of the members who were house surgeons had had as many as six cases. Lawson Tait was not a member of the Society but was invited to come as a guest and take part in the discussions. He got up and stated that he had had either 68 or 86 cases, I do not remember which, he still being a student without any license to practice at all. Various members of the Society expressed their incredulity, but Lawson Tait was quite equal to the occasion and proceeded to give all particulars of cases with the same minuteness as Defoe employed in his history of Robinson Crusoe. After he had given six or eight most vivid accounts of his operations and success the Society thought they would take the remainder as read. . . . There is no particular interest in Laycock's letter, but the man was very interesting personally. He had a most profound confidence in himself and I have heard him say 'Twenty-five years ago, gentlemen, I wrote a book which was then half a century above its age, but the age is now gradually beginning to appreciate it.' The odd thing was that in saying this he understated the truth. The book was 'Nervous Diseases of Women,' and such neurologists as Ferrier and Crichton Browne still look upon it as in advance of the age. Laycock was really the original of Sherlock Holmes. Conan Doyle got the idea from Joe Bell, but Joe Bell got his ideas from Laycock, who was Bell's teacher as well as mine. He used sometimes to make very brilliant diagnoses, and at others, great mistakes. I have known him diagnose waxy degeneration of the capillaries of the small intestine, and post-mortem examination proved the correctness of the diagnosis. He has also been known simply on walking through a ward to look at a man and say 'This patient has cancer of the pancreas.' Again he was correct. One day he was telling the students a great deal about a child and he said to them, 'Gentlemen, I know all this from my observation of the mother.' 'Please, Sir,' said the woman, 'I am only his stepmother.' Another time he was saying, 'This I can tell, gentlemen, from the condition of the patient's teeth.' 'Please, Sir, shall I hand them round?' said the patient, taking the teeth out. . . "

John Hunter's letters to Jenner are good examples of the circumstantial notes of a scientific investigator, wrapped up in his own subject. An amusing instance is the famous letter of September 25, 1778, in which Hunter bluntly consoles Jenner for disappointment in love, "Let her go, never mind her. I shall employ you with hedgehogs." In the Brunton correspondence there is a letter from Gaskell, in which we are taken into his laboratory and

see the great physiologist at work on his monograph on the vagus nerve.

"GRANTCHESTER, CAMBRIDGE,
"April 3, 1882.

"DEAR BRUNTON:

"It was very good of you to think of me with respect to the tortoises. I certainly am going on with the vagus action and have already made a large number of experiments on the tortoise and a few on the snake; every animal has its own peculiarities and affords very interesting results—tortoises are specially good. I hope to work through all the different kinds of beasts I can get and finally tackle the mammal. As to Meyer's tortoise, I think I have seen the same thing to all intents and purposes in the ordinary tortoise. I find the R nerve always has more power of stopping or slowing than the L, while the L often has a more marked action on the strength of the auricular contractions than the R. Also the separation of fibres that slow and fibres which diminish and increase the force of the contractions is carried out by nature in the ordinary tortoise in a most excellent way, for the R vagus first passes to the sinus and is in connection with the ganglion cells there, then in great part leaves the heart to run an isolated course along one of the coronary veins, which passes from the ventricle to the sinus entirely free, so that a piece of nerve lying between the ganglia of sinus and those in auric.-ventr. groove can be isolated and stimulated. The result is that the fibres which pass to the sinus do all the slowing; those which pass to the auric.-ventr. ganglia do the diminution and increase of the auric. contractions. Also, other matters of great interest have turned up, showing for instance that the sequence of vent. upon aur. does not depend on the large nerves between sin. and vent. but upon the auricular contractions. Some of these results I hope to show at Cambridge and would much like to show them to you and talk them over.

"With kind regards to Mrs. Brunton,

"Yours ever,
"W. H. GASKELL."

A note of Lister's refers to his monograph on the cutaneous pigmentary system of the frogs, one of his preliminary studies in the mechanism of inflammation.

"May 28, 1889.

"MY DEAR DOCTOR LAUDER BRUNTON:

"My observations on the pigment cells were published in the *Phila. Trans.* for 1859. May I ask you to accept one of the few separate copies I have left?

"The impression conveyed to me in observing the movements of the pigment molecules was that they were free in a fluid. But we then knew nothing about protoplasm, and I have often felt a desire to observe the phenomena again in the light of our present knowledge.

"Believe me,

"Yours very truly,

"JOSEPH LISTER."

There is an interesting batch of letters interchanged between Sir Henry Acland and the late Dr. John S. Billings, which deserves to be printed in part, if the Acland letters can ever be entirely deciphered. The passage in the Acland note referred to by Brunton (*supra*) reads as follows:

"OXFORD, ENGLAND,

"July 24, 1891.

". . . At last I can see the hope of the foundation here of a general comparative pathology, one of my lifelong dreams for Oxford, through good report and evil report. You must all help me to counteract the craze here to educate *numbers* ONLY for the 'M.B.,' omitting thereby all earlier conceptions of the wider morphology and pathology which John Hunter, one would have thought, had founded forever.

"Always yours,

"H. W. ACLAND."

Among the many unpublished notes of Billings is this breezy little bit of chaffing, one of his humorous love-taps to his personal friends:

"January 5, 1892.

"I have yours of January 4th. I do not in the least understand what you mean by acknowledging the receipt of your 'suspension in the Surgeon General's Department.' Who has been suspending you? What are you suspended from? And why do you feel particularly thankful about it?

"With the compliments of the season,

"Yours very sincerely,

"JOHN S. BILLINGS."

The following, addressed to the Harvard physiologist, Professor Henry P. Bowditch, deals with one of the burning questions of the hour, namely, the centralization of public health in a governmental bureau. It has the bold, straightforward *aller droit au but* which was eminently characteristic of Billings.

"February 27, 1892.

"My Dear Dr. Bowditch:

"Your letter of February 23d is received. I do not upon the whole think that it is desirable to attempt to create a Cabinet officer to be known as a 'Medical Secretary of Public Health'; or that it is expedient for the medical profession to urge the creation of such an office. At best it would be held but four years, and the probabilities of having it filled by a satisfactory man are, I think, extremely small. The benefits to be derived from it are very doubtful. It is the old scheme of Jeremy Bentham. Such an officer, to have any practical power, must have more or less control of the medical departments of the government, that is to say, of the Medical Departments of the Army and of the Navy, of the Marine Hospital Service, the Indian Bureau, the Pension Bureau, of the Army Medical Museum and the Naval Museum of Hygiene, and so on. This is a concentration of powers and duties which I feel very sure would not be expedient at the present time, and it would require a man with the qualities of an archangel to fill the position satisfactorily. I believe that we ought to have a National Board of Health, composed of a limited number of men, such Board to be under the direction of the Department of the Interior, and not of the Treasury Department. But this scheme for a medical cabinet officer appears to me to be utterly impracticable, and in fact hardly worth serious discussion; and I feel absolutely certain that no influence which can be brought to bear upon the present Congress could induce the creation of a new salaried office like this.

"With kindest regards and best wishes believe me to be,

"Very sincerely yours,

"J. S. Billings."

HOMAGE TO SIR WILLIAM OSLER

By Arpad G. Gerster, M.D., New York

ΧΟΡΟΣ

. . . τής ἀνδρείας
Εἵνεκα ταύτης,
Εὐτυχία γένοιτ' ἀν—
θρώπῳ, ὅτι προήκον
'Ες βαθὺ τῆς ἡλικίας,
Νεωτέροις τὴν φύσιν ἀυτοῦ
Πράγμασι χρωτίζεται
Καί σοφίαν ἐπασκεῖ.

Aristophanes, *The Clouds*

CHORUS

. . . virtutem
Ob hanc
Feliciter evenit huic
Homini, quod ætate,
Multum provecta,
Recentioribus ingenium suum
Rebus exornat,
Et sapientiam colit.

Versio Stephani Bergleri (1760)

CHORAL SONG

. . . for virtue's guerdon
This fate is vouchsafed now
To yonder man:
That at the age
Of mellow ripeness
His genius, through wisdom's culture,
May freshly blossom forth in works
Of all-surpassing beauty.

Paraphrase by A. G. G.

EPIDEMICS OF INFLUENZA IN 1647, 1789-90 AND 1807

AS RECORDED BY NOAH WEBSTER, BENJAMIN RUSH, AND DANIEL DRAKE

By Guy Hinsdale, M.D., Hot Springs, Va.

THE earliest record of influenza in America was made by Hubbard, whose "Manuscript"[1] informs us that:

"In the year 1647 an epidemical sickness passed through the whole country of New England both among Indians, English, French and Dutch. It began with a cold and in many was accompanied with a light fever. Such as bled, or used cooling drinks, generally died; such as made use of cordials, and more strengthening, comfortable things, for the most part recovered.

"It seems to have spread through the whole coast, at least all the English Plantations in America, for in the Island of Christophers and Barbadoes there died 5 or 6000 in each of them. Whether it might be called a plague or pestilential fever, physicians must determine. It was accompanied in those islands with a great drought, which burnt up all their potatoes and other fruits, which brought the provisions of New England into great request with them, who before that time had looked upon New England as one of the poorest, most despicable, barren parts of America."[2]

Noah Webster, the famous lexicographer, in his "Brief History of Epidemic and Pestilential Diseases," published in Hartford, Conn., in 1799, in two volumes, gives in chronological order a list of epidemics of "influenza or epidemic catarrh," dating in Europe from A.D. 1174, and in America from 1647. In this remarkable list of 44 instances of influenza there are most interesting notes of earthquakes, volcanic eruptions, and comets, since it was the fashion in those days to associate something supernatural with the outbreak of a pestilence. So we read that the epidemic of 1174 was "the year

[1] William Hubbard's Manuscript, Massachusetts Historical Society "Collections," 2d Series, VI, 531, 532. The author is indebted to Mr. Worthington C. Ford for the transcript.

[2] There is a slight confusion here. According to Winthrop the drought *preceded* the pestilence.—H.

before an eruption of Etna"; that of 1510 "the *same* year with an eruption in Iceland and following great earthquakes, humid air—a comet appeared the next year"; in 1647, "First catarrh mentioned in American annals. The same year with violent earthquakes in South America, a comet."

In Noah Webster's view, Etna, Vesuvius, comets, and earthquakes loom large in etiology. He states[3] in regard to the epidemics listed:

"1. That most of them happened, after or during severe cold, or during moist weather and in spring, winter or autumn. Some, however, occurred in dry hot seasons, and others in mild winters.

"2. Nineteen instances occurred in years when there was a volcanic eruption in Italy or Iceland, and eleven others, though in different years, were within a few months of eruptions; making 30 out of the 44. Two or three others happened near the time of volcanic discharges in South America."

"3. Almost all happened in years of earthquakes, or within a few months preceding or following them.

"4. Thirty instances occurred within the year, or a few months preceding or following the appearance of comets.

"It is further to be observed that some of these epidemics have been limited to the American hemisphere, at the distance of three, four or five years from an epidemic of the same kind in Europe. Such as those of 1647–1655—which coincide in time with violent earthquakes in South America."

It is remarkable and worthy of record that the epidemic of influenza which ravaged the Atlantic coast shortly after the Revolution had practically all the features of the recent epidemic. There was no better student of clinical medicine in those days than Benjamin Rush, who held the chair of the Practice of Medicine and of Clinical Practice in the University of Pennsylvania, which a century later was graced by Prof. William Osler. Dr. Rush had the unusual faculty and patience to set down the minute details of cases as they came under observation. He was deeply interested in the weather as it affected the sick and the well, and he urged his students to make a study of meteorology; this was partly because of the evident relation of epidemic diseases to atmospheric condi-

[3] II, 33–36.

tions. Climatic influences always had for him a prominent place in etiology.

On turning to Rush's chapter on influenza as published in his "Inquiries and Observations," one is struck with a very remarkable parallel between the course of the epidemic of 1789 and 1790 and that of 1918 and 1919. In the account preserved to us by Benjamin Rush there are many of the familiar symptoms so noticeable in the last epidemic.

Rush noticed that the epidemic followed a cool summer and, in the early cases, occurred in those suffering from fatigue. Then follows a classic description of the extraordinary sneezing with hoarseness and sore throat; a sense of weariness, chills and fever, pains in the head, and abscesses in the frontal sinus. Rush noted the watery eyes and the occurrence of swellings just behind the ears, now recognized as the familiar mastoiditis. There was the distressing cough which in some cases was more of a tracheitis; and the final pneumonia. He also described the abdominal form; also the fact that those employed in out-of-door occupations, such as 'longshoremen, surveyors, and the Niagara Indians, had it severely. He notes the occurrence of insanity consequent on influenza. We wonder if Rush could possibly have observed the effects of the streptococcus hemolyticus, for he described "streams of blood" and spitting of blood in consequence of the violence of the cough.

Dr. Rush's account is of great historic interest, revealing a parallel between the clinical course of these two epidemics separated by 129 years; so I am giving his account in his own words.

"AN ACCOUNT OF THE INFLUENZA AS IT APPEARED IN PHILADELPHIA IN THE AUTUMN OF 1789, IN THE SPRING OF 1790 AND IN THE WINTER OF 1791, FROM 'MEDICAL INQUIRIES AND OBSERVATIONS' BY BENJAMIN RUSH, M.D., PUBLISHED IN PHILADELPHIA, 1819.

"The latter end of the month of August, in the summer of 1789, was so very cool that fires became agreeable. The month of September was cool, dry, and pleasant. During the whole of this month, and for some days before it began, and after it ended, there had been no rain. In the beginning of October, a number of the members of the first congress, that had assembled in New York, under the present national government, arrived in Philadelphia, much indisposed with colds. They ascribed them to the fatigue and night air to which they had been exposed in travelling

in the public stages; but from the number of persons who were affected, from the uniformity of their complaints, and from the rapidity with which it spread through our city, it soon became evident that it was the disease so well known of late years by the name of the influenza.

"The symptoms which ushered in the disease were generally a hoarseness, a sore throat, a sense of weariness, chills, and a fever. After the disease was formed, it affected more or less the following parts of the body. Many complained of acute pains in the head. These pains were frequently fixed between the eye-balls, and in three cases which came under my notice, they were terminated by abscesses in the frontal sinus, which discharged themselves through the nose. The pain in one of these cases, before the rupture of the abscess, was so exquisite that my patient informed me that he felt as if he should lose his reason. Many complained of a great itching in the eye-lids. In some the eye-lids were swelled. In others, a copious effusion of water took place from the eyes; and in a few, there was a true ophthalmia. Many complained of great pains in one ear, and some of pains in both ears. In some, these pains terminated in abscesses, which discharged for some days a bloody or purulent matter. In others, there was a swelling behind each ear, without a suppuration. . . . Sneezing was a universal symptom. In some, it occurred not less than fifty times a day. The matter discharged from the nose was so acrid as to inflame the nostrils and the upper lip, in such a manner as to bring on swellings, sores, and scabs in many people. In some, the nose discharged drops, and in a few streams of blood, to the amount in one case, of twenty ounces. In many cases it was so much obstructed as to render breathing through it difficult. In some, there was a total defect of taste. In others, there was a bad taste in the mouth, which frequently continued through the whole course of the disease. In some, there was a want of appetite. In others, it was perfectly natural. Some complained of a soreness in their mouths, as if they had been inflamed by holding pepper in them. Some had swelled jaws, and many complained of tooth-ache. I saw only one case in which the disease produced a coma.

"Many were affected with pains in the breast and sides. A difficulty of breathing attended in some, and a cough was universal. Sometimes this cough alternated with a pain in the head. Sometimes it preceded this pain, and sometimes followed it. It was at all times distressing. In some instances it resembled the chin cough. One person expired in a fit of coughing, and many persons spat blood in consequence of its violence. I saw several patients in whom the disease affected the trachea chiefly, producing great difficulty of breathing, and, in one case, a suppression of the voice, and I heard of another in which the disease, by the falling of the trachea,

produced a cyanche trachealis. In most of the cases which terminated fatally, the patients died of pneumonia notha.

"The stomach was sometimes affected by nausea and vomiting; but this was far from being a universal symptom.

"I have met with four cases in which the whole force of the disease fell upon the bowels, and went off in a diarrhœa; but in general the bowels were regular or costive.

"The limbs were affected with such acute pains as to be mistaken for the rheumatism, or for the break-bone fever of 1780. The pains were most acute in the back and thighs. Profuse sweats appeared in many over the whole body in the beginning, but without affording any relief.

"It affected adults of both sexes alike. A few old people escaped it. It passed by children under eight years old with a few exceptions. Out of five and thirty maniacs in the Pennsylvania hospital, but three were affected with it. No profession or occupation escaped it. The smell of tar and tobacco did not preserve the persons who worked in them from the disease, nor did the use of tobacco, in snuff, smoking or chewing, afford a security against it.

"Even previous and existing diseases did not protect patients from it. It insinuated into sick chambers, and blended itself with every species of chronic complaint.

"It was remarkable that persons who worked in the open air, such as sailors, and 'long-shore-men, (to use a mercantile epithet) had it much worse than tradesmen who worked within doors. A body of surveyors, in the eastern woods of Pennsylvania, suffered extremely from it. Even the vigour of constitution which is imparted by the savage life did not mitigate its violence. Mr. Andrew Ellicott, the geographer of the United States, informed me that he was a witness of its affecting the Indians in the neighborhood of Niagara with peculiar force. The cough which attended the disease was so new and so irritating a complaint among them that they ascribed it to witchcraft.

"It proved most fatal on the sea-shore of the United States.

"Many people who had recovered, were affected a second time with all the symptoms of the disease. I met with a woman, who after recovering from it in Philadelphia, took it a second time in New York and a third time upon her return to Philadelphia.

"Many thousand people had the disease, who were not confined to their houses, but transacted business as usual out of doors. A perpetual coughing was heard in every street of the city. Buying and selling were rendered tedious by the coughing of the farmer and the citizen who met

in the market places. It even rendered divine service scarcely intelligible in the churches.

"A few persons who were exposed to the disease escaped it, and some had it so lightly as scarcely to be sensible of it. Of the persons who were confined to their houses not a fourth part of them kept in their beds.

"It proved fatal (with few exceptions) only to old people, and to persons who had been previously debilitated by consumptive habits. It likewise carried off several hard drinkers. It terminated in asthma in three persons whose cases came under my notice, and in pulmonary consumption, in many more. I met with an instance of a lady, who was much relieved of a chronic complaint of her liver; and I heard of another instance of a clergyman whose general health was much improved by a severe attack of this disease.

"It was not wholly confined to the human species. It affected two cats, two house dogs and one horse within the sphere of my observations.

"In the treatment of the influenza I was governed by the state of the system. Where inflammatory diathesis discovered itself by a full or tense pulse, or where great difficulty of breathing occurred, and the pulse was low and weak in the beginning of the disease, I ordered moderate bleeding. In a few cases in which the symptoms of pneumony attended, I bled a second time with advantage. In all these instances of inflammatory affection, I gave the usual antiphlogistic medicines. I found that vomits did not terminate the disease, as they often do a common catarrh, in the course of the day or a few hours.

"The duration of this epidemic in our city was about six weeks. It spread from New York and Philadelphia in all directions, and in the course of a few months, pervaded every state in the union. It was carried from the United States to several of the West India Islands. It prevailed in the island of Grenada in the month of November, 1789, and it was heard of in the course of the ensuing winter in the Spanish settlements in South America.

"The following winter was unusually mild, insomuch that the navigation of the Delaware was not interrupted during the whole season, only from the seventh to the twenty-fourth of February. The weather on the third and fourth of March was very cold, and on the eighth and ninth days of the same month, the mercury stood in Fahrenheit's thermometer at 4 degrees at seven o'clock in the morning. On the tenth and eleventh, there fell a deep snow. The weather during the remaining part of the month was cold, rainy and variable. It continued to be variable during the month of April. About the middle of the month there fell an unusual quantity of rain. The showers which fell on the night of the seventeenth

will long be connected in the memories of the citizens of Philadelphia, with the time of the death of the celebrated Dr. Franklin. In the last week of the month the influenza made its appearance. It was brought to the city from New England and affected, in its course, all the intermediate states. Its symptoms were nearly the same as they were in the preceding autumn, but in many people it put on some new appearances. Several persons who were affected by it had symptoms of madness, one of whom destroyed himself by jumping out of the window. Some had no cough, but very acute pains in the back and head. It was remarked that those who had the disease chiefly in the breast the last year, complained now chiefly of their heads, while those whose heads were affected formerly, now complained chiefly of their breasts. In many it put on the type of an intermitting fever. Several complained of constant chills, or constant sweats; and some were much alarmed by an uncommon blue and dark color in their hands. I saw one case of ischuria, another of an acute pain in the rectum, a third of anasarca, and a fourth of a palsy in the tongue and arms; all of which appeared to be anomalous symptoms of the influenza. Sneezing, and pains in the ears and frontal sinus, were less common now than they were in the fall; but a pain in the eye-balls was a universal symptom. Some had a pain in the one eye only, and a few had sore eyes, and swellings in the face. In two persons whom I saw, the cough was incessant for three days, nor could it be composed by any other remedy than plentiful bleeding. A patient of Dr. Samuel Duffield informed me, after his recovery, that he had had no other symptom of the disease than an efflorescence on his skin, and a large swelling in his groin, which terminated in a tedious abscess.

"The prisoners in the jail who had it in the autumn, escaped it this spring.

"During the prevalence of this disease, I saw no sign of any other epidemic.

"It declined sensibly about the first week in June, and after the twelfth day of this month I was not called to a single patient.

"The remedies for it were the same as were used in the fall.

"I used bleeding in several cases on the second, third and fourth days of the disease, where it had appeared to be improper in its first stage. The cases which required bleeding were far from being general. I saw two instances of syncope of an alarming nature, after the loss of ten ounces of blood; and I heard of one instance of a boy who died in half an hour after this evacuation.

"I remarked that purges of all kinds worked more violently than usual in this disease.

"The convalescence from it was very slow, and a general languor appeared to pervade the citizens for several weeks after it left the city.

"I shall conclude this account of the influenza by the following observations:

"1. It exists independently of the sensible qualities of the air, and in all kinds of weather. Dr. Patrick Russel has proved the plague to be equally independent of the influence of the sensible qualities of the atmosphere, to a certain degree.

"2. The influenza passes with the greatest rapidity through a country, and affects the greatest number of people, in a given time, of any disease in the world.

"3. It appears from the histories of it which are upon record, that neither climate, nor the different states of society, have produced any material change in the disease. This will appear from comparing the account I have given, with the histories of it which have lately been given by Dr. Grey, Dr. Hamilton, Dr. A. Fothergill, Mr. Chisholm, and other modern physicians. It appears further, that even time itself has not been able materially to change the type of the disease. This is evident, from comparing modern accounts of it with those which have been handed down to us by ancient physicians.

"I have hinted in a former essay at the diminutives of certain diseases. There is a state of influenza, which is less violent and more local, than that which has been described. It generally prevails in the winter season. It seems to originate from a morbid matter, generated in crowded and heated churches, and other assemblies of the people. I have seen a cold, or influenza, frequently universal in Philadelphia, which I have distinctly traced to this source. It would seem as if the same species of diseases resembled pictures, and that while some of them partook of the deep and vivid nature of mosaic work, others appeared like the feeble and transient impression of water colours."

A third epidemic of influenza occurred twenty-seven years after the one described by Rush. We have a brief record by Daniel Drake in his "Systematic Treatise on the Principal Diseases of the Interior Valley of North America." This work, in two volumes of nearly a thousand pages each, was published after his death, and is a monumental record of the history of clinical medicine, as he and his colleagues observed it, during the first half of the last century.

It will be noticed that Drake was acting as an army surgeon to two regiments of militia in camps when the influenza swept down from the East to the frontier post in the Ohio Valley where he was stationed. Drake describes it in these words:

"1. *History*. The cause of this malady is as utterly unknown, as the place where any one of its invasions commenced. I am unable to say how often it has traversed our Interior Valley, for its vast uniformity of surface leads to an extensive production of the endemic disease at the same time, when it is generally called influenza, and the means of distinguishing it from that malady do not exist. It is sufficient to know that we have been invaded by this exotic epidemic.

"The first and greatest invasion of this kind which I have had an opportunity of witnessing, occurred in the year 1807. In the summer or early autumn, the newspapers brought the intelligence of its prevalence in Europe and afterwards that it had reached our eastern cities. It was in October, when the weather was fine and steady that it appeared in this locality. Two regiments of militia called into the field to repel from our frontier a threatened invasion of Indians, were at the time encamped a few miles out of town and I was then in attendance upon them. These men were its first subjects, the people of the town still being healthy. In a few days, however, it reached the latter, and then sought out the scattered inhabitants of the country. At that time there was but little communication between our settlements, yet I was able to ascertain that it 'spread far and wide' among them.

"I need not give the history of any other prevalence, as this illustrates the most constant of the laws which govern influenza; first its progressive extension from east to west; second its independence of all sensible conditions of the atmosphere; third, its first outbreak in bodies of men, and compact settlements.

"2. *Symptoms*. While the symptoms of this new visitant were substantially the same as those of catarrh, there were modifications which deserved notice. Thus, although it often commenced in the nares alone, it seemed at the same time to invade the whole respiratory membrane. There was more fever, and the signs of inflammatory orgasm were often very apparent; but the highest characteristic, not always present, was a sense of sinking and prostration, with a serious feeling of disorder throughout the whole system, indicating the impress of some malignant agent. In subsequent epidemics, I met with cases of the same kind; although they did not prove fatal, they suggested the idea of danger."

Dr. Drake closes his account by noting among the sequels of influenza the occurrence of purulent pleural effusions and the unusual number of cases of pulmonary phthisis that developed.[3]

[3] The magnitude of the recent epidemic of influenza has not been fully measured, but it seems to have exceeded any previous one of which we have a record. The London *Times* has stated that the deaths in the entire world have numbered twelve millions. We have no means of corroborating this estimate, but it is believed that the deaths in the United States have reached over 500,000. In Canada in 1918 there were 13,880 deaths in a total of 53,700 cases of influenza. Late reports give the mortality in India alone at three millions.

VOTUM MEDICI

UT CONATA MEA SINE RATIONE LUCRANDI
AUT PERDENDI PERFICIAM.
UT SERVIAM SINE EXSPECTATIONE
GRATIAE FAMAEVE.
UT IUVEM MAGIS QUAM IUBEAM.
UT MAGIS CIRCUMVENIAR QUAM CIRCUMVENIAM
FIDEIQUE DESIM.
UT ONUS OFFICI SUSCIPIAM POTIUS, ET MUNERIBUS
QUAE AD ME ATQUE AD HOMINES PERTINEANT
MAXIME PERFUNGAR QUAM MIHI IPSI
COMMODUM MAGNUM CAPIAM.
UT VIRES ET SCIENTIAM AD OPUS EFFICIENDUM
HABEAM QUODCUNQUE DI MIHI DENT.
UT NIL QUERAR.
UT CONSTANS, FIDELIS AMANSQUE SIM.
UT OMNIA SORDIDA ET MALA ODERIM SINE
ACERBITATE ERGA EUM QUI PECCET.
UT FATUM INELUCTABILE FORTITER OPPETAM.
UT MINISTRATIONEM SOLITUDINIS, SILENTI ET DOLORIS
MENTE OBSTINATA ACCIPIAM.
UT MODERATE, PALAM, TEMPERANTER VIVAM—
HAEC OMNIA SINT MIHI VOTA COTIDIANA.

By Bayard Holmes, M.D.,
Chicago, Ill.

SIR WILLIAM OSLER AND THE JOHNS HOPKINS HOSPITAL

HOW SIR WILLIAM OSLER PROMOTED AND FOSTERED THE ACTIVITIES OF HIS STUDENTS AT THE JOHNS HOPKINS HOSPITAL, 1889–1905

By Henry M. Hurd, M.D., Baltimore, Md.

THE Johns Hopkins Hospital of Baltimore was opened in May, 1889. Although Dr. Osler was appointed Physician-in-Chief in 1888, he did not remove to Baltimore until the following year. The opening of the hospital for the reception of patients had been much delayed because of the expectation, unfortunately not realized, that the Medical School of the Johns Hopkins University would be established in connection with it. An attempt had already been made to arrange courses of study at the Johns Hopkins University to prepare students to enter upon the study of medicine when H. Newell Martin was appointed Professor of Biology, and later when William H. Welch became Professor of Pathology in 1886. After spending a year abroad in special study, Dr. Welch took up his residence in Baltimore in 1887. Laboratory accommodations were thereupon provided for him in the Pathological Building of the Johns Hopkins Hospital, and the teaching of students began there in 1888. Here he formed classes and guided the work of special students, inaugurating laboratory instruction which proved of great value, not alone to Baltimore, but to the country at large, when the newer methods of bacteriology and pathology were first presented to medical students. At the opening of the Hospital no further effort was made at first to inaugurate systematic instruction in medicine. In the autumn of that year, however, largely through the initiative of President Gilman of the Johns Hopkins University, who had co-operated in the organization of the hospital, courses were announced and classes were established for post-graduate students. Such classes were well attended and

averaged between fifty and seventy-five students each year until the establishment of the Medical School in 1893. They served a useful purpose, and were among the earliest facilities afforded to students in the United States to become familiar with bacteriology and the modern methods of medical investigation.

Dr. Osler took up his residence at the hospital during the first year, and was surrounded by a busy company of young medical men, many of them recent graduates in medicine, who were eagerly engaged in laboratory work or medical study and investigation.

In October, 1889, through the hearty co-operation of Doctors Welch, Osler, Halsted, and Kelly a Medical Society was established which has continued in uninterrupted operation for the past thirty years. At the meetings of the society medical and surgical cases from the hospital or dispensary were presented and terse and instructive comments were made upon them. Formal papers upon new or interesting medical topics, followed by more or less formal discussions, were features of the society. The moving spirit in its organization was Dr. Osler, who attended its meetings with great regularity, and engaged actively in its work. The meetings were held in the library of the hospital, and were attended not only by members of the staff and post-graduate students, but also by representatives of the medical profession in Baltimore. The society soon outgrew the limited space furnished by the library and its sessions were later transferred to the medical amphitheater. At these meetings were presented the results of original studies in malaria, tuberculosis, amebic dysentery, diphtheria, typhoid fever, neuro-histology, and various branches of more special and newer methods of laboratory work. Meetings were held twice monthly during the university year, and proved a great source of interest and profit to the students, as will be seen by the reports in the *Bulletin* of the hospital and the papers printed in detail therein.

Soon after at Dr. Osler's suggestion, a Journal Club was established, which met weekly in the afternoon or evening, and furnished an opportunity for all who were interested to acquaint themselves with the newest medical literature. Internes and students were appointed to present summaries of the current literature in the various branches of medicine. Papers were read sometimes *in extenso;* generally, however, summaries were presented. The effect

upon the student body was excellent, and all students were thus stimulated to keep themselves in touch with the current medical journals of America and Europe. The Journal Club soon created an appetite for medical literature.

In the following year, at the suggestion of Dr. Osler, the Historical Club was established, which held a monthly meeting, and gave an opportunity to students to become familiar with the history of medicine. This club has held regular meetings during the past twenty-nine years. At first, a series of formal and scholarly papers was presented on the various aspects of the writings of Hippocrates. Later, similar papers were read upon the writings of Celsus and other classical writers. Largely through the initiative of Dr. Osler, careful sketches were given of the earlier physicians in England and America. The list of Osler's own papers is a long one, and includes such titles as "An Alabama Student," "Influence of Louis on American Medicine," "John Keats, the Apothecary Poet," "Oliver Wendell Holmes," "Thomas Dover, M.B., of Dover's Powder, Physician and Buccaneer," and others. The meetings of this society attracted physicians from other parts of the United States, and many interesting papers upon historical topics connected with medicine were thus brought before the students: and many of them were published in the *Bulletin* of the Johns Hopkins Hospital.

Another student activity which Osler initiated was the Laënnec Society, for the study of tuberculosis. This grew out of his effort to familiarize himself with the extent of the prevalence of tuberculosis in the city of Baltimore. At his own expense he employed two medical students to follow up dispensary cases of tuberculosis at their homes, to study housing conditions, and to ascertain and to remedy the defects existing in the home care of tuberculous patients. The condition thus brought to his attention by the efforts of his students proved to be so serious as to decide him to begin a systematic movement in the community towards more varied and effective work for the detection of tuberculosis and its relief. He further desired to place a knowledge of the dread disease thoroughly before the public, and to interest physicians generally in the early detection of the disease and its prompt treatment. Hence, the Laënnec Society was established, and held regular meetings at the

hospital during Dr. Osler's residence in Baltimore, and has continued them since his departure in 1905.

It is of special interest to recall the fact that Dr. Osler's energetic and enthusiastic work in organizing and directing the Laënnec Society soon came to the knowledge of Mr. Henry Phipps of New York, who, unsolicited, placed in Dr. Osler's hands a liberal fund for the fuller prosecution of this work. The out-patient work at the Johns Hopkins Hospital thus made possible became so useful that Mr. Phipps eventually established the Phipps Dispensary for the treatment of tuberculosis. This dispensary was inaugurated first in a small building adjoining the General Dispensary; it subsequently was much enlarged by two generous contributions from the same liberal donor, and has since accomplished a remarkable work in the detection, diagnosis, and treatment of early tuberculosis in Baltimore and its vicinity.

All of these societies have performed an important work in leading many medical students to devote themselves to medical research and investigation in every department of medicine.

In conclusion it should be added that beyond and above all other influences exercised by Dr. Osler was the daily and hourly spectacle of his tireless industry as a teacher, writer, and student of medicine, and his boundless enthusiasm over the rapid progress of medicine, his generous recognition of the efforts of others, his unselfish assistance to those who were struggling to advance it, and his unfeigned pride in their success. During the whole period of his residence in Baltimore he was the guide, friend, and elder brother of his students. He welcomed them to his hospitable home and regularly gathered them in larger or smaller groups to read with them the newer literature, to discuss the problems of medicine, or to present some project of social betterment. He gave freely of his time and energies to all who came under his notice, and ever had an open hand for all who needed aid. His presence and example were a benediction to all.

AN APPRECIATION OF HERMANN WEBER

By A. Jacobi, M.D., New York

HERMANN WEBER was a lifelong friend of mine. I knew him first at Bonn in 1849, after having left the University of Goettingen in 1849. My sojourn at Bonn lasted from my sixth semester, 1849 to 1851, where after my eighth semester I was graduated in medicine in April, 1851.

Hermann Weber was born December 30, 1823, of a German father and an Italian mother. His early years were spent in country life in Bavaria and Hesse-Cassel, and he studied in Fulda until he left for the University of Marburg. Here he met Carlyle during his medical studies. From Marburg he changed to Bonn, where his relations with Englishmen were still more frequent. It was here that Sir Peregrine Maitland, Sir Henry Havelock, and Sir James Simpson gained an influence on the active young man. It was through them that his studies of Shakespeare, and of English in general, became more matured and his English future more established.

It was in Bonn that he graduated in medicine, 1848, and built the foundation for his future greatness, his position there being that of first assistant of the medical clinic of the university. As such, he prepared the lectures of the professor, Friedrich Nasse, for whom he was the superintendent of the medical clinic. In that capacity he controlled the clinic-dispensary work, which, under Nasse, was quite extensive, the number of patients from the poorer classes treated at the clinic being very large, consisting of adults and children, both surgical and medical cases. All the advanced students were in charge of patients, in great part responsible work. The professor himself participated in the active work, which was guided by the actual assistants, whose activities were many. The students were occupied many hours every day, and their labors did not end with the death of the patients, as our school work was not closed until the post-mortem and epicrises were finished.

The most important factor in my labors in Bonn was the method-

HERMANN WEBER.

ical teaching at the university. There was but one instructor in Germany comparable with Nasse, namely, Krukenberg of Halle. Indeed these two clinics were the only thorough ones in German universities. These two professors were actually in contact with French teaching. We students were fully aware of what was going on in France under Laennec and Piorry, and were quite superior in attainments to the students in Vienna, where Skoda taught and Rokitansky demonstrated.

It is characteristic in the life of Hermann Weber that while he continually studied and learned, he never ceased to teach. I early adopted his methods, and never forgot them. I learned from him to combine the study of the case and the obligation to the human creature when treating a patient, and I applied his theories in later life when teaching. My connection with American teaching institutions was of the same nature, both scientifically and humanistically. I have been assured that my influence as a general teacher has been the result of what was inculcated by my lifelong friend and teacher, Hermann Weber. There should be more such friends and more such teachers.

His first public position in England was that of house physician in the German Hospital of Dalston, a general hospital in London, where I met him a few times after I landed in England as a refugee. Meanwhile I felt that our paths had diverged considerably. He had applied for admission to the Royal College of Physicians, of which, after studying in Guy's Hospital, he became a member at the same time as Dr William Odling, in 1855. About that time he joined the "Medical Society of Observation," which attracted all the younger men—his co-workers—of the London profession; and from that time dated his friendship with Addison, Edmund Parkes, Wilson Fox, Hilton Fagge. It was in 1894 that he established the "Weber-Parkes Prize" for the study of tuberculosis, which has been awarded five times altogether.

"Tuberculosis," "phthisis," "consumption" were his lifelong topics of study and close exertion. The British profession has not failed to recognize this. On the Council of the Royal College of Physicians he served as a censor in 1879 and 1880. The honor of knighthood came to him in 1899. He became a consulting physician to the Royal National Hospital for Consumptives at Ventnor; to

the North London Consumption Hospital; and to the King Edward VII Sanitarium. He was connected with a great many British and foreign learned societies. All must have been sources of intense satisfaction to him, but the keenest interests of the warm-hearted man were his lifelong sympathies with poverty, sickness, and humanity.

A great many of Weber's publications may be found mentioned in the two series of the Index Catalogue of the Surgeon General's Office, Vols. XVI of the 1st, and XXI of the 2d series. Extensive writings of his form part of Ziemssen's Cyclopædia of 1880, of Quain's Dictionary, and of Allbutt and Rolleston's "System of Medicine." His Croonian lectures before the Royal College of Physicians in 1885 treated extensively of phthisis, like others of his special studies. His "Notes on the Climate of the Swiss Alps" (1864), his "Treatment of Phthisis by Residence in Elevated Regions," belong to this class.

Many results of his studies were embodied in an extensive book published with his son, Dr. F. Parkes Weber, the last edition of which, "Climato-therapy and Balneo-therapy," appeared in 1907.

An obituary published in the *Lancet*, of December 7, 1918, speaks of him in warm words. The claims of climatology were publicly recognized owing to his knowledge of the subject, Hermann Weber being an ardent mountain climber all over the Alps and Apennines. His recommendations of Switzerland, Tyrol, and Italy, and wintering in high altitudes were generally well known. His adventures in the Alpine Club were matters of extensive knowledge. In his sixty-eighth year he climbed the Wetterhorn and the Jungfrau; in his seventy-third year he still made extensive Alpine trips. He did not give them up until he reached his eightieth year. They made him the great judge "amongst half a dozen of British prime ministers and a number of members of the royal English family." One of my personal letters from him, which was burned in a fire September 20, 1918, speaks enthusiastically of his tour up Mount Sinai "a few years previously."

He was medical officer to the Central office of the North British and Mercantile Insurance Company for many years; was president of the Life Assurance Medical Officers' Association from 1897 to 1899; and his presidential address on heredity in relation to life

assurance showed considerable prevision in respect to matters that have since become subjects of more elaborate discussion and arrangement.

In connection with his extensive active and scientific studies, those on the muscular tissue are easily appreciated.

His main care was the treatment of the muscular tissue. In his last paper[1] he referred to much of what he had taught for decades: The principal movements ought to be those of walking, but arms should be exercised similarly, not only of the young, but of the old, always in relation to the different ages and conditions. Friar Roger Bacon knew that the body heat decreased after the age of forty.

The effects of the muscular actions on different parts of the body are pointed out, as follows:

1. Increased afflux of blood to the muscles with each contraction.
2. Increased nutrition of the muscle combined with improved metabolism and production of body heat.
3. Increase of exchange of fluid between blood and tissues.
4. Facilitation of the removal of waste products.
5. Preservation of the elasticity of the thorax and lungs.
6. Abundant supply of oxygen for the blood and the metabolism.
7. Maintenance of the healthy condition of the organs of circulation, from the heart to the smallest arteries, capillaries, and lymphatics.
8. Massage of the bones, keeping up the healthy condition of the bone substance and the bone marrow, and through this the formation of a sufficiency of blood efficient for the fight with hostile bacteria entering it.
9. Increase of the resisting power of the body against disease.
10. Persistence of the working capacity of the brain centers, which initiate the action of the different sets of muscles.

This last paper of his is characterized by assiduity, like every one of his endeavors. Even when he participated in the "Festschrift in honor of A. Jacobi, M.D., LL.D.," 1900, p. 14, in his "A Contagious Form of Pneumonic Fever in Children," he displayed the same exactitude. Even in his last article he extended general knowledge regarding patients of advanced years.

Hermann Weber died November 11, 1918.

[1] "On the Influence of Muscular Exercise on Longevity," *Brit. M. J.*, Feb. 23, 1918.

EDWARD JENNER, A STUDENT OF MEDICINE, AS ILLUSTRATED IN HIS LETTERS

By Henry Barton Jacobs, M.D., Baltimore

THE 17th of May, 1919, marks the 170th anniversary of the birthday of Edward Jenner. The great contribution to public health and happiness which this man made has not only stood the challenges and criticisms of time and men, but stands to-day as the most momentous of all prophylactic measures against disease which has yet been suggested. The magnitude of his one great contribution so completely engrosses our thoughts of Jenner, at least in the mind of the present generation, that all other ideas of his personality or of his work are quite eclipsed, and so it has occurred to me that it might be appropriate in this, the 170th returning year of his birth, to recall by quotation from a few of his own letters some of the other medical subjects which engaged his attention, and in which he also made distinct contributions to medical knowledge.

Moreover, the fact that this paper is one of many others offered as a token of esteem and affection on his birth anniversary to another, younger by just an hundred years, and whose earliest medical contribution also related to smallpox, seems further to make the subject appropriate.

Space and opportunity together compel but a limited number of quotations from those letters at hand. It is believed that some, at least, have never before been published, and to that extent are of particular interest.

Care has been taken to avoid as far as possible quotations relating to the discovery of vaccination. For the sake of simplicity the letters are arranged in chronological sequence.

In reading these extracts the state of medicine in Jenner's time must be constantly borne in mind. He lived in the early period of the great medical awakening at the end of the eighteenth and the beginning of the nineteenth century. In Britain, Huxham, Cullen, the two Hunters, Heberden, Fothergill, Lettsom, Baillie, Parry;

in France, Corvisart, Pinel, Bayle, Bichat, Andral, Laënnec, Louis, and Piorey, together formed a group from which modern medicine has its origin.

Jenner fortunately enjoyed in his student years the instruction, inspiration, and friendship of John Hunter, that great investigator and seeker after Nature's secrets. To him he owed, largely perhaps, his love for the study of natural phenomena, though he must have possessed an innate tendency in that direction, and a curiosity to solve problems in Nature much greater than that which moves most young men.

The following letter from Hunter to Jenner indicates that Jenner had already, at an early date, undertaken investigations of his own, and had become interested in surgical lesions which were also of interest to the London surgeon.

Mr. Hunter to E. Jenner.[1]

DEAR JENNER: I received your account of your experiments on the hedge-hog, also the dog-fish, for which I thank you. I have now received your account of the aneurismal vein with the cast, and showed it to my pupils this evening with the description.

I hope you will be able to procure the arm when the man dies. If you would choose to have it published, I would either give it to the Medical Society here, or send it to Edinburgh to be published in their commentaries. Let me know your inclination, and I will add whatever I may think wanting, and give it your name. I am very happy to hear that some of you have wished to communicate your ideas to another. If I can give you any assistance, command me; I shall always be glad to hear from you as an individual, or as from the Society. Mrs. H. desires her compliments to you. Have you left off fossilizing?

I am, dear Jenner,

Your much obliged and humble servant,

JOHN HUNTER.

London, April 28th.

In May, 1777, in writing to Jenner, John Hunter mentions his own indisposition, with which he had suffered from time to time since 1773, and in August he went to Bath for the waters, where Jenner saw him. Jenner at once concluded that Hunter's

[1] Baron's "Life of Edward Jenner," I, 47.

trouble was due to the angina pectoris, the disease from which he was to die sixteen years later.

So much impressed was Jenner with the seriousness of Hunter's complaint that soon after he wrote to Heberden as follows:

E. Jenner, to Dr. Heberden, 1778.[2]

SIR: When you are acquainted with my motives, I presume you will pardon the liberty I take in addressing you. I am prompted to it from a knowledge of the mutual regard that subsists between you and my worthy friend Mr. Hunter. When I had the pleasure of seeing him at Bath last Autumn, I thought he was affected with many symptoms of the Angina Pectoris. The dissections (as far as I have seen) of those who have died of it, throw but little light upon the subject. Though in the course of my practice I have seen many fall victims to this dreadful disease, yet I have only had two opportunities of an examination after death. In the first of these I have found no material disease of the heart, except that the coronary artery appeared thickened.

As no notice had been taken of such a circumstance by anybody who had written on the subject, I concluded that we must still seek for other causes as productive of the disease: but about three weeks ago, Mr. Paytherus, a surgeon at Ross, in Herefordshire, desired me to examine with him the heart of a person who had died of the Angina Pectoris a few days before. Here we found the same appearance of the coronary arteries as in the former case. But what I had taken to be an ossification of the vessel itself, Mr. P. discovered to be a kind of firm fleshy tube, formed within the vessel, with a considerable quantity of ossific matter dispersed irregularly through it. This tube did not appear to have any vascular connection with the coats of the artery, but seemed to lie merely in simple contact with it.

As the heart, I believe, in every subject that has died of the Angina Pectoris, has been found extremely loaded with fat, and as these vessels lie quite concealed in that substance, is it possible this appearance may have been overlooked? The importance of the coronary arteries, and how much the heart must suffer from their not being able duly to perform their functions (we cannot be surprised at the painful spasms) is a subject I need not enlarge upon, therefore shall only just remark that it is possible that all the symptoms may arise from this one circumstance.

As I frequently write to Mr. H. I have been some time in hesitation respecting the propriety of communicating the matter to him, and should be exceedingly thankful to you, Sir, for your advice upon the subject. Should it be admitted that this is the cause of the disease, I fear the medical

[2] Baron's "Life of Edward Jenner," I, 39; I, 47.

world may seek in vain for a remedy, and I am fearful (if Mr. H. should admit this to be the cause of the disease) that it may deprive him of the hopes of a recovery. . . .

Here, then, is the first intimation that angina pectoris, described by Heberden in his "Commentaries on the History and Cure of Diseases," is at least partially dependent upon coronary artery disease for its occurrence.

Heberden had found only "small rudiments of ossification in the aorta" in the one case he had examined post-mortem. In Osler's seventeen post-mortems, recorded in the eighth edition of his text book, thirteen presented coronary artery disease. We must conclude, therefore, that this is the predominating lesion in angina pectoris, and to Edward Jenner's careful observations must be given credit for its discovery—a fact which modern medical historians admit.

In the letter following one finds that as early as 1790 Jenner had become interested in hydatid disease, particularly of the kidneys, and had suggested a remedy. Full report of the case, as made before the Gloucestershire Medical Society, July 28, 1796, is to be found in *British Medical Journal*, May 23, 1896. Jenner thought the patient improved under use of turpentine, and it was administered because the general opinion seemed to be that hydatids were insects.

Whether or not Jenner accepted Hunter's reasoning that the hydatid was an animal rather than an insect we are left somewhat in doubt. We know, however, this was but the beginning of his inquiries into the nature of this parasite, as letters to come will show.

Mr. Hunter to E. Jenner.[3]

DEAR JENNER: I have just received the favour of yours. I have just now forgot the case of hydatids; but if there was any thing that struck me, I dare say it was laid by. They are frequently in the kidneys, but I should doubt your oil of turpentine having any merit in bringing them away. My reason for supposing them animals is because they move after they have been extracted. I have taken them out of the head or brain of a sheep, and they have contracted in different parts of them when put into warm water. I should be glad to employ you if I knew in what; but if any thing comes across my imagination, I will think of you. The measly pork are hydatids.

[3] Baron's "Life of Edward Jenner," I, 39; I, 47; I, 98.

I am afraid of your friend Mrs. L. There is a hard tumour that almost fills the pelvis, most probably the uterus. How does Mrs. Jenner do? do you bring her to London? What family have you got? My compliments to Mrs. Jenner, and believe me to be, dear Sir,

Your most obedient, and
Most humble servant,
JOHN HUNTER.

December 8th, 1790.

The next letter from Sir Everard Home, son-in-law, executor, and successor of John Hunter, is interesting as confirming in Hunter's case the ideas Jenner had formed regarding angina pectoris. Such a complete substantiation of his diagnosis, made sixteen years before, must have been gratifying, though in the loss of his friend he was deeply grieved.

Sir Everard Home to Dr. Jenner.[4]

LEICESTER SQUARE, February 18th, 1794.

MY DEAR SIR: I have sent you by the Major the numbers due to you from the Royal Society. I am well assured that you were sincerely afflicted at the death of your old and most valuable friend, whose death, although we all looked for it, was more sudden than could have been imagined. It is singular that the circumstance you mentioned to me, and was always afraid to touch upon with Mr. Hunter, should have been a particular part of his own complaints, as the coronary arteries of the heart were considerably ossified.

As I am about to publish a life of Mr. Hunter, which will contain both the symptoms of the disease, and the dissection, I shall not say more about it at present; it will be prefixed to the work on inflammation, and we hope to have it printed at the end of next month.

I cannot say that I have met with the ossification of these arteries so frequently as other alterations of structure in the heart, but this case is very much in favour of your theory. . . .

Throughout his life Jenner maintained firmly that the digestive organs, particularly the stomach, were in the animal economy the main source of good or ill health. Here again he anticipates many a later advocate.

The following letter puts this belief in picturesque words. It also indicates that diseases of the eyes, "these invaluable organs," had claimed his thoughts.

[4] Baron's "Life of Edward Jenner," I, 39; I, 47; I, 98; I, 104.

CHELTENHAM, Octob^r. 8th, 1797.

WM. PETER LUNELL, Esq.,[5]

Bristol.

MY DEAR FRIEND: . . . The hour may come (I do not despair of its arrival) when my stomach, where, wielding an absolute Sceptre, sits the grand Monarque of the Constitution, may undergo some spontaneous change, which may meliorate its present condition; and then I trust you will find me a more orderly correspondent, and that William Shakespear may furnish me with a better motto than that which is now, alas, too applicable "To morrow, to morrow & to morrow." . . . And pray how are your Eyes?—My little lecture on this subject did not sufficiently catch your attention. I know not why; for the preservation of this invaluable organ has occupied much of my Time, & perhaps the most intense of my Studies have been devoted to it.

Believe me

Y^s. very faithfully

EDW. JENNER.

Osler says, in his article on acute endocarditis, that "Bouilland first emphasized the association of simple endocarditis with rheumatic fever. Before him, however, the association had been noticed."

Bouilland, living from 1796 to 1881, published his researches on articular rheumatism and the coincidence of pericarditis and endocarditis with this disease in 1836.

The letter which follows shows that Jenner already had written a paper on this subject prior to 1805. As a matter of fact, on July 29, 1789, "Mr. Jenner favored the Society with Remarks on a Disease of the Heart following Acute Rheumatism, illustrated by Dissections." (Record of the Gloucestershire Medical Society.)

From the wording of the letter one would certainly infer that the observations on the relation of the heart to rheumatism were original ones, and that to Jenner therefore belongs the credit of first noticing this relationship. The Fleece Medical Society was another name for the Gloucestershire Medical Society, as it met in the parlor of the Fleece Inn, Rodborough, Gloucestershire.

[5] From Dr. Jacobs' collection.

BERKELEY, Jan^{y}. 10th, 1805.

DR. PARRY,[6]
Circus, Bath.

DEAR PARRY: . . . A neighbour of mine died yesterday from a disease of the Heart, which followed two or three severe attacks of acute Rheumatism. You may probably remember a paper of mine that was given into the *Fleece Med. Socy.* on this subject. This & my other Papers are in your possession. If you would be good enough to convey them to me, I should be extremely happy in regaining them particularly that I now allude to, as I am confident many a life is lost by not shielding the Heart at the going off of acute Rheumatism, which not unfrequently at that time feels a morbid determination of blood. . . .

Yrs. truly,

E. JENNER.

The next letter indicates that Jenner formed early a sane, if perhaps radical, view of the value of medicinal baths.

WILLIAM LUNELL, Esq.,[7]
Bristol.

MY DEAR SIR: . . . Now my good sir, what shall we do? I am almost tempted to say, will not Miss Wait be benefitted by a change of scene, at least by that of changing the air of Bristol—a murky City, for the aether of Cheltenham? Our Springs too might prove salubrious. In the days of old you know, we could reckon but on one, now we boast of eleven. Our Chalybeate Spring rivals that of Tunbridge, and our sulphurated Spa, the famous water of the North. It is really a very extraordinary fact that all the medicinal waters of any celebrity in the Island are to be found concentrated in this little spot, Bath excepted, and to this I attach no more value than that which flows from my Tea Kettle. . . .

Believe me,

Truly yours,

EDWARD JENNER.

CHELTENHAM, 5th Jan^{y}. 1811.

The appreciation of the value of comparative anatomy and pathology may have come to Jenner from his master, John Hunter; at any rate he was a believer in it, as he testifies in the two following letters, written only a day apart in 1813, when sixty-four years old. They indicate how interested he still was in the hydatid disease, and how well his enthusiasm for investigation persisted.

[6] From Dr. Jacobs' collection.
[7] *Ibid.*

The language is poetic, but evidently the author here confuses the two hepatic diseases, cirrhosis and hydatids. However, the desire for greater knowledge is most praiseworthy.

The letter to "My dear young Friend" is such a beautiful one that it is quoted in full.

I would have it noted that Jenner's mind here is surely contemplating an active agency as the source of infection in typhus. Reference to this will be made later on.

BERKELEY, March 14, 1813.

DR. MORGAN,[8]

Great Russell Street,

London.

MY DEAR FRIEND: . . . I have not been in town since the summer of 1811, nor much at Cheltenham, preferring, whenever I am permitted, the enjoyment of my Cottage in this, my native Village. But don't think I spend my time in idleness. My pursuit has lately been, when uninterrupted by Vaccination, the morbid changes in the Structure of the Livers of Brutes, which has led me to some conclusions respecting the same changes in the human. Tis hard methinks that the poor animal that is content with what the meadows afford for his daily Bill of Fare & whose Cellar is the Pond or the Brook, should perish from the same diseases as the Drunkard; but so it is. There are Plants which some how or another are capable of throwing the state of the Liver into that sort of confusion which calls Hydatids into existence. These do not continue long in their native state, but produce a great variety of Tubera, cartilaginous, boney masses, &c. In other instances the disease originates in the biliary Ducts which become astonishingly enlarged & thickened in every part of the Liver and finally destroy it in various ways. This is the outline of my research. The Hydatid I can call into existence in the Rabbit in about a fortnight. . . .

Your much attach'd

EDW: JENNER.

BERKELEY, March 15, 1813.

MY DEAR YOUNG FRIEND: Before I received a confirmation of your convalescence under your own hand & seal, I had the happiness of hearing of it thro' one of your relatives here. Be assured it was a great happiness:

[8] From Dr. Jacobs' collection.

for had the Monster Typhus stuck one of his venom'd Fangs so deep as to have wounded you mortally, I should have griev'd exceedingly. What is this Fellow—into what apartment of our Mansions does he first break in, and how does he perform the work of havock? Let this form one of the subjects of our conversation when next we meet. I have both seen and felt enough of this burglarious Depredator to excite a wish to detect him in his first hiding place where he makes his entry & think I have found him out. I have been endeavoring to trace him by means of my old auxiliary, analogy—but no more of this now, except a hint respecting the oxymuriatic gas. On this as the best contrivance to stop his rambling from place to place, I have a very confidential reliance. Let me entreat you to keep a watchful eye over yourself for some time to come. The activity of your mind may outstrip the powers of your Muscles and keep up a state of debility, which would be overcome by a due quantity of rest. Your Father's Letter tells me how imperiously you are call'd upon to attend to this. I should say some lounging amusement would be the thing for you. A long journey is out of the question, otherwise, I should say, come and take it here; at all events when you are able I shall hope to see you. I hear much of Mrs. Ibbetson's beautiful Discoverys among vegetables with her microscope. Who would have thought that the Nettle concealed for so many ages such treasures for the Naturalist. Have you seen its spiral apparatus for darting forward its sting when irritated by the touch? How beautifully the God of Nature displays to us his great and grand Museum. Were all the doors to be thrown open at once, our senses would be confused & on recovery we sh^{d}. be satiated, just like those (comparing small things with great) who exhibit the Gallerys of Napoleon.

I am still going on with my inquiries into the causes and effects of the morbid changes of the Liver in Brutes. This has led me into some conclusions respecting the same morbid changes in the structure of that Viscus in the human body. How wonderful that the poor animal whose Larder is the Meadow and whose Cellar is the brook should perish from the same diseases as the Drunkard; but so it is. There are plants which somehow or another are capable of throwing the Liver into that kind of confusion which calls Hydatids into existence. These vermin do not continue long in their natural state, but produce a great variety of Tubera in all manner of shapes and forms. They are variously organiz'd; fleshy, boney, cartilaginous, etc. In other instances the disease originates in the deranged state of the biliary Tubes, from one extremity of the Liver to the other, which become astonishingly enlarged in their diameter, & thickened. Hence such havoc arises that Hydrops Pectoris is the consequence, emaciation & death. Accept this as just an outline of my research, which from a thousand inter-

ruptions, and I must confess from a dislike to application, has been conducted in a very desultory way.

Pray let me hear soon how you are going on, & thank your Father for his letter.

Believe me, my dear Henry, very truly

Yours,

Edw. Jenner.

? Henry Cline.[9]

It may be recalled that Mrs. Jenner for the greater part of her married life was an invalid, suffering from a chronic pulmonary complaint, with an occasional hemorrhage; that Dr. Jenner's eldest son died of consumption, following the death, from the same disease, of his young tutor, who had lived in the house. It is no surprise, therefore, that Jenner should have been extremely anxious about his younger and only remaining son. The three following extracts relate to this boy's health. They show a keen appreciation of the early symptoms of pulmonary tuberculosis, the insidious nature of its onset, and the value of fresh air in its treatment—differing only from the modern teaching in believing that its temperature should be regulated.

Cheltenham, Dec^r. 2, 1813.

Mr. R. Jenner,[10]
Henley, Oxon.

My dear Robert: . . . We should have been extremely happy to have heard by him that you were looking well but we were griev'd to hear that you look'd pale & thin. When you left us you were stout & in good health. Pray tell me, are you entirely free from Cough, or Complaints about your chest of any sort or kind? Such as a sense of tightness or difficult breathing or using any great exertion? Have you at any time a pain in your side under the Ribs? Are your bowels got back to the old state of costiveness? Don't fail to tell me, if you are unwell the precise feelings you experience.

I trust you diligently attend to all I have said again & again about cold.

The Post is going out & I can only add with what anxiety & affection I remain

Truly Yours,

E. J.

[9] From Dr. Jacobs' collection.
[10] *Ibid.*

MR. R. JENNER,[11]
Henley, Oxon.

DEAR ROBERT: You would not have had another Letter so soon had it not been for your telling me that your Cough still continues. In my opinion you cannot have recourse to the remedy too soon; however, at all events call on Dr. Routh. The sort of Cough you had when here, is sometimes more troublesome to cure, & is apt to continue longer than when it attacks at once with greater severity. . . .

Yr. affte. Father

E. JENNER.

Decr. 20, 1813.

DR. WORTHINGTON,[12]
Southend
near Upton.

MY DEAR DOCTOR: . . . My poor dear Robert came home from School about ten days since with a bad Cough & looking so peculiarly ill, so like his lost Brother, that I was almost struck dead at his appearance. Thank God! he is already much better & his Cough nearly gone. Our sheet anchor in threatening cases I believe is the constant breathing of air duly regulated as to temperature. One very cheering circumstance is, his not having a quick pulse.

Most truly Your's

EDW: JENNER.

The next letter quoted opens up fully the question of Jenner's conception of tubercle. In the letters describing his researches upon hydatids in the livers of brutes he speaks of "tubera" being formed, and here he writes of another "tubercle" bursting. It is probable that the words relate in some sense to pathological processes, which, to Jenner, seemed more or less identical, though we are not to suppose that either represents the true tubercle of Laënnec. That there must have been some kind of relation between the tubera from hydatids and the tubercle of consumption in Jenner's mind is evident, for in a letter to the Rev. Dr. Worthington, of December 13, 1809, quoted in Baron, II, 407, Jenner says: "What dreadful strides pulmonary consumption seems to be making over every part of our Island. I trust some advantage may, one day or another, be derived from my having demonstrably made out that what *is* tubercle in the lungs *has been* hydatid."

[11] From Dr. Jacobs' collection. [12] *Ibid.*

While there existed this unquestioned confusion in Jenner's conception of the etiology of consumption, I cannot but believe that he had a glimmering of the truth that consumption was dependent upon the introduction into the lungs of some active, living substance, and, to this extent, he was a forerunner in thought to all those who since have demonstrated the exact state of the case. The former letter, relating to typhus, still further substantiates my idea that he was searching in the right direction in his effort to explain infection.

It may be well to remark here what Hektoen has called to attention, namely, that in Jenner's "Inquiry," published in 1798, he gives, in the words of Garrison, "an early reference and a clear explanation of anaphylaxis or allergy. In Case IV, he notes that inoculation of variolous matter in a woman who had had cowpox thirty-one years before, produced a palish red efflorescence of the skin, which he regards as almost a criterion of whether the infection will be received or not, attributing the phenomenon to the dynamic of a permanent change in the blood during life."

CHELTENHAM, Sept^r. 22, 1814.

CH^s. MURRAY, Esq^r.,[13]
Bedford Row,
London.

MY DEAR SIR: After the accounts you must lately have heard from this place respecting the health of poor Gen^l. Lyman you will not be surprised at the doleful intelligence I now communicate. It was evident yesterday that he was in a dying state, & this afternoon at ten minutes past one, he expired without a groan or a struggle. The Miss Lymans bear the loss with as much firmness as one can expect. I understand the family in Town will be appriz'd of the event by this Post.

The General's state of health continued nearly stationary from the time of his arrival here till the commencement of the late warm weather, soon after which he declined rapidly & another Tubercle burst about a week since, which discharged profusely.

Pray make my best Compt. to Mrs. Murray & yr. Family & believe me very truly Your's

EDW. JENNER.

In the letter which follows, at the age of sixty-seven, we still find him interested in anatomy and evidently engaged in some research involving the lymphatics.

[13] From Dr. Jacobs' collection.

DR. BURDER,[14]
21 Southampton Row,
Russels Square, London.

MY DEAR SIR: . . . You speak of your engagements—I hope they are of a nature to afford you pleasure & that professional calls are already occupying part of your time, as a reward for your attentions & laborious exercises during your long residence in Scotland. I could wish you for a moment to turn to your Notes on the Lymphatics, & just tell me whether anything new is said of their structure—If I recollect right a lymphatic has two Coats, the external less delicate than the internal.

Believe me, with best wishes, dear Sir

Very truly yrs.

EDW. JENNER.

BERKELEY, Feb. 5th, 1816.

Here are Jenner's views regarding wine and its effects upon the human system—a timely subject for discussion at the present day.

BERKELEY, March 2, 1816.

R. F. JENNER, Esq^r.,[15]
Exeter College, Oxford.

MY DEAR ROBERT: Your last Letter relieved me from an anxiety naturally felt respecting your health, for you express'd yourself more vaguely in your Letter than in your quotation, as in the former nothing was said about your having taken a Cold, but that you were unwell; so I was left to guess at the nature of your indisposition. I trust you have attended to my suggestions with regard to the Wine, & that you have only sent for a sufficiency for present use. You will be coming home ere long & we can talk more about the *poisonous* business when we meet. You know my fixt & unalterable opinion of wine, as far as regards its deleterious effects on the human constitution. . . .

Yr. affectionate Father

EDW^d. JENNER.

A picturesque letter in which he anticipates animal experimentation in physiology:

BERKELEY 31 August 1816.

DOCTOR CHARLES PARRY, M.D.[16]
Gay Street, Bath.

MY DEAR CHARLES: . . . with regard to Pathology.

The impression at present on my mind is that somehow or another the milk of the mother is capable of receiving impregnations which affect

[14] From Dr. Jacobs' collection. [15] *Ibid.* [16] *Ibid.*

the child. We have not yet made out *all* the odd things going forward in the animal economy. Tell me how it comes to pass that if I drink a glass of good cider my urine smells as fragrant as the bottle when just uncorked? I don't give this as a parallel case but as a puzzle. There must be a short cut from the stomach to the Bladder. Shall we ask Riddle about these things? What if we were to fill the Stomach of a Puppy with Mercury first tying up the Intestine and then give it a good squeeze? . . .

Ever yrs.

my dear F-[d]

Edw[d]. Jenner.

This interesting letter to his friend, Dr. Parry, is quoted in full as the finale to this paper. The freshness of mind and spirit is delightful, despite his more than sixty-seven years; note, too, his wisdom in prescribing diet to the new-born babe—anticipating completely the modern modified milk treatment—and again recurring to his doctrine that the stomach is the key to health. Note, too, his search for truth and his rejection of terms inexpressive of true processes, his realization of the youthfulness of scientific research, and the great fields which yet lay ahead for investigation.

'Tis at once the letter of the young enthusiast and the resigned expression of one who realizes fully that his day is over, and is content to await the future whatever it may bring—with complete *Aequinimitas*.

Chauntry Cottage, Berkeley, Oct. 15, 1816.

Dr. Charles Parry,[17]

Gay Street, Bath.

My dear Charles: I am happy in writing to you, & making *for me*, rather a quick reply to your last letter. The beauty of my God-daughter must be secur'd at all points & I have sent her the enclos'd little present to guard her from the spells of the Fiend that takes delight in spoiling Ladys faces. Mr. Norman had better use the points on the arms of some Cottage children, and having produc'd a Pustule (vesicle if it must be so) to vaccinate from that. I mention this because the Lymph fresh from the arm is more certain than when inspissated, even (as per experiment) tho' it has not been dried five minutes. Emma I think had but one Pustule, which I fancy went thro' its course undisturb'd—However, it w[d]. do the Lady no harm to *test* her from her sister's arm. The matter sent is fresh

[17] From Dr. Jacobs' collection.

from as fine a Pustule, as ever was call'd up by Vaccine Lancet. Some Dolts, Walker of Oxford and Shinlake of Taunton have lately been writing some alarming stuff in the Yellow Journal declaring thro' thick and thin that all the V. matter now in use is worn out by being work'd so long. Pretty analogy this—"the world is young." Now the fact is, that this par nobile had got some that was ruined from contamination by some individual whose skin (from disease) was incapable of producing that which was correct. This sort of decompos'd rubbish, I am sorry to say, gets into the hands of the ignorant and produces local disgrace. "The world is in its infancy."

The question is, respecting the stomach in the nursery, whether that is in fault, or whether Mrs. Parrys milk is in a state fit to meet its powers of digestion? I should think the latter, & to put the thing to issue, I w^{d}. have you give the little one a meal or two, from a new milk-pail. The substitutes for milk I believe are all bad. The best deviation I have found from the maternal milk is that of the ass—the next is the Cows diluted with one third part of water, with a very small portion of sugar. But not unfrequently the process of Vaccination acts like a charm in correcting deviation in the absorbent system, & you know it is a doctrine in my school, that the Stomach is the first—the root, the foundation, the governor of the whole family. Away with the term Scrofula—Let us have something expressive of morbid action, or disease of the Lymphatics. You know how long I have been an Hydatid-Hunter & tho' Time has brought me to a hobble, yet I scramble after my Game as hard as I can, And what do you think? I seem to see him now popping out of a Lymphatic, A speck, or specks (small hydatids) appear where a like portion of the Lymphatic is lost. "The world's a Baby."

I don't take in the Institution Journal, but both the others. I must see this paper on the Metals, because you say 'tis good. How goes on Geology? I think I have made out something about the pebbles in our Basaltic-amygdaloid Rock. I wish you would look at your Oolite thro' a good magnifyer. I find—(stop—I fancy so) they are made up of concentric layers; the first crystaliz'd on a small atom, a fragment of stone. You really should see, with a geological eye, the Country around this place—the diversity it presents would delight you, and if my good old Friend in the Circus would but accompany you, then after a day's hunt we w^{d}. sing old Rose & burn the Bellows. I really want to sing a swan-like ditty to him before————I want too, to write to him; but when I think of setting about it my head seems so full, I know not how, and so it is put off until to morrow, to morrow & to morrow.

"The world's a Fœtus." Adieu my dear Charles—Bob & Catherine desire their best affections with myself to you, Mrs. Parry & the accomplished Miss Emma.

Most truly yrs

Edwd. Jenner.

P.S.
No Cheltenham for me, this
winter.

THE INFLUENCE OF OSLER ON AMERICAN MEDICINE

By George M. Kober, M.D., LL.D., Washington, D. C.

DR. OSLER has passed his seventieth goal post. Sincere personal appreciation of the master work of this chieftain in the art and science of medicine, gratitude for the kindly inspirations experienced through his influence, and the sanguine hope that his fair example may stimulate the younger generation to emulate his noble achievements have prompted the writer to lay the wreath of tribute at the feet of this most deserving of septuagenarians.

Early Life and Student Days. Sir William Osler was born at Broad Head, Ontario, July 12, 1849, the son of F. L. Osler, a clergyman of the Church of England. His were not only rare physical and mental characteristics through parental inheritance, but, as told him by his old and true friend, Dr. Jacobi, at the farewell banquet tendered to him on May 2, 1905, "It is no mean felicity to be born with the imprint of virtue."

Those familiar with the portrait of Osler as a schoolboy at Trinity College, and those fortunate enough to have been personally associated with him in later years, have read in that face innate qualities which not only endeared him to his friends, but, in the estimate of his dear old mother, "were more precious than all his honors."

Osler's earliest school life was passed in the school of his native village, following which he went to Port Hope for a term or two in Trinity College School of that place, and later still he entered Trinity University at Toronto. Devoted to his books during hours of class, he enjoyed his play with the "playful child let loose from school." Robust of health, his mind matured with equal pace.

On quitting Trinity College young Osler entered the office of Dr. Bovell at Toronto as assistant, and there he inaugurated his medical studies, later matriculating in the School of Medicine of McGill University, Montreal, graduating in 1872.

We learn from his classmate, Professor F. J. Shepherd, that while a conscientious worker, Osler never passed for "a grinder." He was not particularly known for his devotion to books, nor were his efforts entirely focused towards success in examinations, but his main attention was directed towards the post-mortem room and to all hospital work within reach. He was beloved because of his social qualities, kindliness of disposition, and characteristic sense of humor. Dr. Shepherd remarks:

"While he did not graduate very high in his class, there is a note in the convocation that a special prize was awarded for his graduation thesis, because of the originality it displayed and the research it evinced, and because of the collection of pathological specimens accompanying it which were presented to the museum. In the light of his after studies, it is interesting to note that some of these specimens, still in the college museum, concerned the ulcers of typhoid fever."

As a student, Osler was deeply interested in comparative pathology, and as teacher in subsequent years often illustrated a point in human disease by a reference to a parallel condition in the lower animals.

How carefully he prepared himself for the practice of medicine and the professor's chair is evinced in the fact that following his graduation he spent two years abroad in study in the laboratory of the physiologist, Burdon-Sanderson, and attending the clinics of Jenner and Wilson Fox, Ringer and Bastian in medicine and the dermatological clinics of Tilbury Fox. In 1873 he took the degree of licentiate of the Royal College of Physicians in London. Thereupon he went to Berlin, where he studied pathology under Virchow, physiological chemistry under Salkowsky, and clinical medicine under Frerichs and Traube. In the early part of 1874 he continued his studies in Vienna under Bamberger, Hebra, and other noted clinicians.

Teacher at McGill University. Upon his return to Montreal in 1874 he was appointed, at the early age of twenty-five, professor of the institutes of medicine at the McGill University, which included the course of physiology and a series of twenty lectures on pathology. In 1875–76 instruction in histology and demonstrations in physiology were added to his work, and the following year a summer course in pathological histology. Dr. Osler served from

1874–75 as Physician to the Smallpox Hospital of Montreal, and it is chronicled that he sacrificed his salary for the purchase of microscopes for his department at the University. Osler himself has said that a man should come into internal medicine by one of three ways —physiological chemistry, physiology, or morbid anatomy. He made himself proficient in all three of these branches, especially in pathology.

In the winter of 1875–76 his autopsy work began at the Montreal General Hospital, and continued for eight years with 1000 autopsies to his credit. In 1878 he was appointed physician to this hospital, and there began his career as a brilliant clinical teacher. A man with such firm scientific foundations, a comprehensive knowledge of the subject presented by him, and his personal magnetism, could not fail to command the respect and esteem of his students and professional colleagues. He not only awakened interest and enthusiasm in modern scientific medicine among his hearers, but also among the members of the medical societies. Even before the completion of his thirtieth year he figured as a leader, and his influence was felt not only in Canada and the States, but merited for him later the appointment of Regius professor of Oxford University. Osler's recollections of his early teaching career are charmingly and modestly set forth in an address delivered at the opening of the session of that school, September 21, 1899, twenty-five years after the faculty, as he declared, "with some hardihood selected a young and untried man to deliver lectures in the Institutes of Medicine."

"My first appearance before the class filled me with tremulous uneasiness and an overwhelming sense of embarrassment. I shall not forget the nice consideration of my colleagues and the friendly greetings of the boys, which calmed my fluttering heart. One permanent impression abides—the awful task of the preparation of about 100 lectures. After the ten or twelve with which I started had been exhausted, I was on the treadmill for the remainder of the session. False pride forbade the reading of the excellent lectures of my predecessor, Dr. Drake, which with his wonted goodness of heart, he had offered. I reached January in an exhausted condition, but relief was at hand. One day the post brought a brand new book on physiology by a well-known German professor, and it was remarkable with what rapidity my labors of the last half of the session were lightened.

An extraordinary improvement in the lectures was noticed, the students benefited, and I gained rapidly in the facility with which I could quote the translated German. Four years later I was appointed on the visiting staff of the Montreal General Hospital. What better fortune could a young man desire? I left the same day for London with my dear old friend, George Ross, and the happy days we spent together working at clinical medicine did much to wean me from my first love. From that date I paid more attention to pathology and practical medicine and added to my courses, one in morbid anatomy, another in pathological histology, and a summer class in clinical medicine. I had become a plurist of the most abandoned sort, and by the end of two years it was difficult to say what I did profess, and I felt like the man to whom Plato applies the words of the poet:

> 'Full many a thing he knew
> But knew them only badly.'

"Weakened in this way, I could not resist when temptation came from pastures new in the fresh and narrower field of clinical medicine. After ten years of hard work I left Montreal a rich man—rich in the treasures of friendship and good fellowship, and those treasures of widened experience and a fuller knowledge of men and manners which contact with the bright minds in the profession necessarily entails. My heart, or a good bit of it at least, has stayed with these treasures."

University of Pennsylvania. In the summer of 1884 Osler received a call from the University of Pennsylvania. When the invitation to present himself as a candidate for the position of professor of clinical medicine at Philadelphia reached him at Leipzig, Dr. Osler told us he was inclined to believe it a joke. Nor was he disabused of this notion until two weeks later a cablegram reached him to meet Dr. Weir Mitchell in London. He added with his characteristic humor, "Boston measures men by brains, it is said, New York by 'baw-bees,' and Philadelphia by breeding." It was Mitchell's task to test his breeding. He did so by having him eat cherry pie, and noting how he disposed of the stones. As Osler disposed of them discreetly, the breeding question was settled.

In 1884 Osler was elected to the Fellowship of the Royal College of Physicians of London, and in 1885 was also chosen from the newly elected fellows of the College to deliver the "Gulstonian Lectures," a singular honor which he most efficiently discharged, selecting for his subject, "Malignant Endocarditis." His lectures

were based on his studies and material available in Montreal. No wonder that a man so highly honored by the Royal College had been chosen the year before to become an associate of Leidy, Pepper, Stillé, and other leading lights. Osler's advent in Philadelphia marked a turning point in the methods of teaching medicine, not only in Philadelphia, but in the States.

In Philadelphia, as in Montreal, as was well said by his friend, Dr. James G. Wilson, he inspired his students with a craving for knowledge based upon facts of the ward, of the microscope, of the laboratory, of the post-mortem room, and also stimulated their interest in medical literature. He demonstrated how medicine should be learned and taught.

He also insisted with the younger generation, by precept and example, that it is not necessary for every physician to be a practitioner in the ordinary sense, but that long years of hospital and laboratory work constitute a better equipment for the teacher and consultant.

Johns Hopkins Medical School. In 1889, at the age of forty, Osler was invited to Baltimore to take charge of the Medical Clinic of the Johns Hopkins Hospital. From this time on dates clearly his greatest activity and usefulness in professional work.

Professor William H. Welch advises us that, when Dr. Osler came to Baltimore, the main intention of the faculty was that the hospital should form an integral part of the medical school, and that opportunities should be afforded for higher clinical training. It accordingly seemed expedient that students should be made part of the hospital machinery, and to Osler is due the credit of working out the details of the scheme. This, indeed, represents his contribution to medical teaching in America.

Influence on Higher Medical Education. Over forty published essays and addresses bearing upon medical education and medical history are sufficient warrant of Osler's keen interest in this subject.

He was ever a staunch advocate of higher pre-medical education requirements, extension of the period of professional study and the substitution of laboratory instruction for didactic teaching. In his "Essay on the Need of Radical Reforms in the Methods of Teaching Senior Students" he advises teachers "to give to students

an education of such a character that they can become sensible practitioners."

Dr. Osler was convinced that it is the duty of a medical school to see that the senior student "begins his studies with the patient, continues them with the patient, ends them with the patient, using books and lectures as tools, means to an end." He persistently maintained that the ideal hospital is one connected with a medical school, with the professors members of the attending staff. In this connection he writes:

"The work of an institution in which there is no teaching is rarely first class. It is, I think, safe to say that in a hospital with students in the wards the patients are more carefully looked after, their diseases are more fully studied, and fewer mistakes are made."

Osler's methods of teaching clinical medicine fitted in admirably with the general policy of the Faculty that the students should be made a part of the machinery of the hospital. As a result the clinical unit was maintained in the fourth year as taught by him, but the work transferred from the out-patient department to the wards. In Osler's judgment

"Each man should be allowed to serve for at least half of the session in the medical wards and half in the surgical wards. He should be assigned four or five beds, and under the supervision of the house physician, he does all the work in connection with his own patients. One or two of the clinical units are taken around the wards three or four times a week by one of the teachers for a couple of hours, the cases commented upon, the students asked questions, and the group made familiar with the progress of the cases. In this way the student gets a familiarity with disease, a practical knowledge of clinical medicine, and a practical knowledge of how to treat disease."

Though Dr. Osler disclaims any credit for his teaching method, it is nevertheless unquestionable that, had it not been for his wonderful personality, enthusiastic and effective leadership, American medical education might still be fifty years in arrears of that of Europe. It required a man of his broad vision, sound judgment, a devotee to his profession, and a statesman in medicine to make converts to the cause of his revolutionary ideals.

Dr. Osler has always felt justly proud of his connection with the organization of the medical Clinic of the Johns Hopkins Hospital and the introduction of the old-fashioned methods of practical instruction, and regards this, "as by far the most useful and important work he has been called upon to do." We who are familiar with the beneficent effects of his individual influence upon his students know that he never failed to do his best work and to keep far afield in every department of medicine, but over and above all this and his breadth of culture and broadminded attitude towards medical problems, he possessed attributes which are rarely found associated in any other single individual.

His was the power of encouraging and inspiring, of firing in the youthful heart an enthusiasm for a chosen life work. The scenes enacted with his students in the out-patient department are fondly recalled. There he stood, surrounded by his boys, lending them friendly advice in some puzzling case. With his arms thrown about their shoulders, through friendly inquiry, marked with occasional humorous interspersions, he guided them on to a satisfactory solution of every difficult problem. Exact always, but never dogmatic, he could not but be always loved, always revered.

We feel that we would be omitting an important page in the story of Osler's activities were we to pass over in silence those homely Saturday evening gatherings, held at the table round in his magnificent library, or those charming essays on medical history, which Sudhoff estimated "to contain more of the historical spirit than many learned works of the professional historian."

These gatherings also enabled him to familiarize himself with the individuality of each student, and in his charming way to offer timely and valuable suggestions as to how to solve certain intellectual and moral problems. Johns Hopkins Medical School has become known as the mother of medical teachers, and since 213 of the 483 graduates prior to 1907 were also his pupils, are or have been connected with our medical schools, it is easy to infer the extent of his beneficent influence.

Dr. Osler realizing, as every master mind necessarily must, the value of example, ever inculcated on his student body esteem for the general practitioner and old-style country doctor. Most of his pupils will cherish gratefully the words addressed to them:

"Many of you have been influenced in your choice of a profession by the example and friendship for the old family doctor or of some country practitioner in whom you have recognized the highest type of mankind, and whose unique position in the community has filled you with laudable ambition. You will do well to make such a man your example, and I would urge you to start with no higher ambition than to join the noble band of general practitioners. They form the very sinews of the profession—generous-hearted men, with well-balanced, cool heads, not scientific always, but learned in the wisdom of the sick room, if not in the laboratories."

Osler was deeply interested in the progress of American Medicine, and proud of its achievements, as shown in his address delivered at the opening of the Museum of the Medical Graduates College and Polyclinic in London on July 4, 1900, in which he pointed out the silent revolution which had taken place in medical education, and especially in the cultivation of the scientific branches, hospital equipment, and clinical facilities.

"The most hopeful feature is a restless discontent which, let us hope, may not be allayed until the revolution is complete in all respects. Meantime, to students who wish to have the best that the world offers, let me suggest that the lines of intellectual progress are veering strongly to the West, and I predict that in the twentieth century the young English physician will find his keenest inspiration in the land of the setting sun."

It is quite natural that a man with such high hopes and aspirations would strongly resent any interference with the legitimate and humane methods employed for the advancement of scientific medicine. I shall never forget the expression of scorn in his eyes and the words with which he rebuked the enemies of scientific progress, who had been heard before the U. S. Senate Committee on a bill for the further prevention of cruelty to animals.

"The blood just surged in my veins, sir, when I heard two men address you to-day who said things which they should have been ashamed to say of the medical profession, of men who daily give their lives for their fellows. . . . With reference to men who train with these enemies of the profession, I say this, that I scorn them from my heart."[1]

[1] See "Hearing on Vivisection," February 21, 1900, Government Printing Office, Washington. The Bill failed in the Committee and no serious attempt has been made to enact what Osler characterized as "a piece of unnecessary legislation."

Influence on the Profession at Large. The many invitations extended and accepted by Dr. Osler to address medical societies attest the savory widespread influence his career wielded over the medical community at home and abroad. His text, "Principles and Practice of Medicine," graces the bookshelves of well-nigh every English-speaking physician the world over.

The medical societies, the efficient vehicle, as he took it, for the dissemination of scholarship, ever received his heartiest encouragement. Accordingly, we find him either enrolled as an active member of these societies or fostering their foundation because, as he said to the members and friends on the occasion of the centennial celebration of the New Haven Medical Association, January 6, 1903, "The Society is a school in which the scholars teach each other, and there is no better way than by the demonstration of the more unusual cases that happen to fall in your way." Through these societies he awakened interest in post-mortem work, the presentation of pathological specimens, and in library equipment. Through them, also, he emphasized what a well-equipped and properly manned hospital in every town of 50,000 inhabitants could effect towards the advancement of clinical medicine. Through them he felt that America would accomplish more for clinical medicine in five years than Germany could in ten.

Osler was one of the most active founders of the Association of American Physicians, organized at a meeting held in the office of Dr. Francis Delafield, New York City, October 10, 1885. Others present at this time were Drs. Wm. H. Draper, Wm. Pepper, James Tyson, George L. Peabody, and Robert T. Edes.

The first scientific meeting of the Association was convened in Washington, June 17, 1886, and from that meeting until his departure for Oxford he was recorded absent from the meetings but twice. Even after his departure, he attended several meetings and was elected an honorary member in 1912. In 1894 he was elected President of the Association, and in his address delivered May 30, 1895, he spoke in part as follows:

"At the opening of our Tenth Meeting the question is timely—How far has the Association fulfilled the object it had in view? Have our aspirations and hopes of 1885 been realized? We sought, as stated in Article I of our Constitution, the advancement of scientific and practical

medicine. With this primary object we sought also, as Dr. Delafield said in his opening remarks, 'An Association in which there will be no medical politics, and no medical ethics; an Association in which no one will care who are the officers and who are not, in which we will not ask from which part of the country a man comes, but whether he had done good work, and will do more, whether he has anything to say worth saying and can say it.'"

Osler believed that the nine volumes of the Transactions offered a full and satisfactory answer to the first question, and referred to them as "the repository of very much that is best in American medical literature." He emphasized the widespread and effective interest which the papers of Dr. Fitz on Appendicitis and of Dr. F. M. Draper on Pancreatic Hemorrhage had produced, and succinctly reviewed some of the topics presented for discussion, such as typhoid fever, the parasites of malaria, tuberculosis, diseases of the gastric intestinal tract, diseases of the heart, blood, blood vessels, kidneys, etc. He boldly stated that several papers had been presented which indicated that the readers had failed to grasp the scope of the Association. He declared that the Association had already shown a powerful influence on the study of pathological and clinical medicine in this country, that there was at present an actual scarcity of trained pathologists and bacteriologists and a distinct need of well-trained special clinical physicians, and of such physicians and of pathologists and bacteriologists should the Association in greater part be composed.

He referred to the limited membership, and with characteristic frankness declared, "We should all understand that this is a working society, and when any one of us ceases to attend regularly, or when our interest grows lukewarm, we will promote best the common welfare by quickly retiring."[2]

Osler was a member of the Council of the Association for a number of years, and exercised a strict but just censorship over the admission of members; he was doubtless the most active worker in that body, as shown by ten original contributions and his discus-

[2] The membership of the association in 1886 was limited to 100, which was increased in 1897 to 125, in 1904 to 135 active and 25 associate members, and further increased in 1912 to 160 active and 25 associate members. Active members after ten years' service may be transferred to the list of emeritus members. Honorary membership is limited to 25.

sion of sixty-four papers presented by other members. He was as popular as a teacher among his colleagues in the Association as with his classes in the medical school. The young and the old were attracted, inspired, and improved, and men like Jacobi and others much older than he had told him that they were glad to sit at his feet and listen to him. Since the majority of these men were occupying professorial chairs, the sphere of his influence has been greatly widened. He was also an enthusiastic founder of the National Association for the Study and Prevention of Tuberculosis in 1904, and has been the Honorary Vice President ever since 1905.

When Osler, well-nigh fifty years ago, stood upon the threshold of his professional life, he stood there convinced of the dignity and responsibilities of his lofty vocation. He stood there convinced that if his name were to be dug deep in the marble walls of the hall of fame, it had to be dug therein with the chisels of study, honesty, and truth. He has now lived a lifetime of life and lived it well. He has lived a lifetime of study, as evinced by over 240 contributions to medical literature. He has lived a lifetime of service to his fellow man, to which bear witness his contributions to preventive medicine, his active participation in the eradication of preventable disease, his kindly ministrations to the sick poor. He has lived a lifetime which has been an honor to his profession and a glory to his professional brethren—a lifetime which has been rewarded with every honor and trust at home and abroad which the medical community could possibly bestow upon him. He has lived a lifetime of service, and during this lifetime he has tempered tenderness with firmness, condescension with authority. His only protest against cares was silence. Dignity met his responsibilities, equanimity his successes and griefs, sufferings and disappointments. And as our congratulations go out to him there follows the sincere hope that his days of activity and bliss may still be many to complement this lifetime that shall know no death.

SERVETUS NOTES

By Leonard L. Mackall, New York

WRITERS on Servetus, almost without exception, seem to be pursued by some singular fatality leading to bibliographical inaccuracy—the most learned become illogical, and even professional bibliographers like van der Linde become careless for the occasion. Hence I hope that the following informal notes,[1] as being based entirely on study of the rare original documents and accepting nothing on mere hearsay, will prove of value by correcting and supplementing various statements still current.

The Portrait of Servetus. There is much uncertainty about portraits of Servetus. Willis's preface states expressly that the portrait prefixed to his book was concocted by the author's daughter, yet it was selected for reproduction by Odhner, 1910. Bernigeroth's engraving in Mosheim, 1748, is crude, so that Sterling ("Some Apostles of Physiology," 1902), Osler,[2] and Garrison naturally preferred Fritzsch's frontispiece in Allwoerden's "Historia," 1728 (not 1727, cf. Mosheim's letter, 1728, at end of most copies), which is re-engraved anonymously in the Dutch version of 1729. Allwoerden explains (p. 132f.):

"Imago haec eius satis accurate expressa est ex antiquo & nitide picto ἀρχέτυπῳ, quod probabile est aliquem ex Serveti amicis fieri curasse, cum in custodia detineretur,"

and that the original painting had belonged successively to Joh. Crellius, Count Schwerin, Stenger, Teuber (Bishop of Halberstadt)

[1] They have now become mere notes on notes! Though written solely for this volume in honor of Sir William Osler, I have since abridged the MS. very materially in order to make room for other contributors. However, I hope to print it later in full, perhaps in the *Annals of Medical History;* and hence should greatly appreciate any corrections or additions for such future use.

[2] Sir William Osler's "Servetus," Oxford, 1909, now out of print, but reprinted the same year in the *Johns Hopkins Hospital Bulletin* for January, 1910; also translated into German in the *Deutsche Revue* for December, 1909, but without the illustrations, which had, however, been retained in the *Bulletin*, and reappear in Hemmeter's interesting paper in *Janus*, 1915, from the original blocks, though differently combined.

and then to Peter Ad. Boysen (author of the "Historia M. Serveti," Wittenbergae, 1712) who lent it to Mosheim. Allwoerden quotes a long letter from Boysen on the subject. That painting seems now permanently lost, and Fritzsch's print is only less crude than that of Bernigeroth. But Allwoerden, who had perhaps seen the original as well as heard about it from Mosheim, fortunately gives us his opinion of the previous engravings thus:

"Ceterum duplex alia Serveti imago nobis occurit aere satis eleganter expressa. Altera in minori folio formæ circiter octavæ descripta erat: Sed exemplo, quod nobis videre licuit, nec chalcographi nomen, nec aliud quid adiectum erat. Alteram vero Christophorus de Sichem in patente charta Amstelodami, adiuncta Serveti historia aut potius accusatione, anno 1607 expressit." (p. 133, cf. Mosheim, p. 241f.)

The admirable article on Servetus in the new Encyclopædia Britannica by the Rev. Alex. Gordon, who has made exhaustive researches into everything connected with the subject, states: "The only likeness of Servetus is a small copperplate by C. Sichem, 1607 (often reproduced)," and so he neatly reproduced this small head in an oval as frontispieces in his privately printed "Personality of Servetus" (Manchester, 1910, cf. the crude drawing in Cuthbertson, p. 52) from the British Museum copy of the "Grouwelen der vornaemster Hooft-Ketteren," Leyden, 1607.[3] This little Dutch book, consisting of short notices and portraits of select heretics, was reprinted several times, in various languages. So much for the small head.

The Uffenbach-Tronchin copy of the larger engraving (extending to the waist) examined by Allwoerden (who reprints the Dutch text below it) and Chauffepié (Nouv. Dict. Hist. IV, 227, cf. Yair's English translation of this Life, 1771) seems to have disappeared entirely. The Geneva Library and Tronchin's family know nothing of it. But the British Museum and I have the "Iconica et historica

[3] Some copies at least of the 1607 "Grouwelen" have only eight portraits, but the German version (Leyden, 1608) has seventeen, and so has the Latin "Apocalypsis insignium aliquot Hæresiarcharum" by "H.S.F.D.M.D." (Leyden, 1608), and the very similar "Speculum Anabaptisti Furoris" (Leyden, 1608). The English translation by John Davies, "Apocalypsis: or the Revelation of certain notorious Advancers of Heresie," was first issued as appended to the second edition (1655) of the "Pansebeia, or, a View of all Religions of the World," by that polemical ubique Alex. Ross (who had even ventured to attack the Religio Medici in his "Medicus Medicatus," 1645). Both the Dutch and English versions were reprinted several times, in cruder form.

Copper-plate Engraving of Servetus. By C. van Sichem (1607).
From Copy in the Surgeon General's Library, Washington

descriptio præcipuorum hæresiarcharum per C. V. S. [i.e., Christoffel van Sichem] Arnheim, 1609," and I am fortunately able to reproduce here an impression[4] with German text in the Surgeon General's Library, van Kaathoven Collection (cf. Index Cat. III, 289, First Series). No doubt it was taken from the "Historische Beschreibung und Abbildung der fürnehmbsten Haupt-Ketzer. Durch C.V.S.A. zu Amsterdam, bey Niclauss, Buchhandler, 1608." The plate itself is the same as in the Latin edition, and doubtless the 1607 Dutch one also (cf. Nagler XVI, 346). It corresponds closely to Allwoerden's frontispiece and evidently the small head of the "Grouwelen," etc., was merely taken out of this careful engraving, which is thus our best substitute for the lost original painting from which it was made. There is no reason why we should not, with Menendez y Pelayo ("Hist. de los Heterodoxos Españoles," II, 312, 1880), consider this portrait as at least "probablemente autentico."

The First Two Publications of Servetus. The genuine original editions of the 1531 and 1532 volumes on the Trinity (printed by Johann Setzer in Hagenau near Strassburg) have for centuries been so extremely rare that it is not surprising that Osler, Cuthbertson, and Hemmeter give an illustration of a counterfeit instead. Fortunately I own the genuine Girardot de Préfond-MacCarthy-Bohn-Thorold copy of both bound together in red morocco, bought by the elder Quaritch personally at the Syston Park sale in 1884. Nodier's well-known story, "Le Bibliomane" (Paris, ou le Livre des Cent-et-un, I, 1831), expressly mentions this very copy as sold in the MacCarthy auction (1817), but carelessly assumes its identity with the Hoym-La Vallière copy. There can be no possible doubt as to its authenticity, and both title-pages are now reproduced in the exact size of the originals.

There has long been great confusion as to the spurious counterfeits of these two books. The counterfeits have a single ordinary hyphen in the words TRINI-TATIS and DIALOGO-RUM on the titles, instead of the two diagonals of the originals now illustrated.

[4] The heading, "Michael Servetus, ein Spangiard," has been cut from the upper margin. Cf. J. K. F. Knaake—auction cat. III, No. 975 (21–23 Febr., 1907, Osw. Weigel, Leipzig) and Hiersemann's cat. 346, No. 1378.

On account of its size, the text ("Michael Servetus . . . Gott wolle Richter sein." 24 lines) and ornamental border are not reproduced in the present volume, but they will be included if these Notes are printed in full.

DeBure's Bibl. Instr. I, 1763, is the only direct authority for any edition of either book with two horizontal lines instead of one, and he does not even mention any edition with only one; so that it is quite safe to disregard his statement as being merely inaccurate. There seems no reason to doubt that the usual counterfeit with the misprint: CHHRSTUM, on p. *83b* (first noted by Ebert, then Graesse; not mentioned in Brunet) of the 1531 book was made for the Rev. Georg Serpilius (1668–1723), a prominent clergyman and learned hymnologist of Regensburg (about 1721?). The 1532 book was evidently reprinted at the same time. The printed catalogue of the library of Serpilius includes copies of "*zweyerley* editiones" of both these books, and also of the very rare 1607 Roman Index, which he likewise counterfeited,[5] expatiating on its rarity in his "S. S. Verzeichnüss einiger Rarer Bücher," I Stück, Frankfort and Leipzig, 1723, pp. 52–72. This is certainly very significant, and we may well believe that he gradually sold the counterfeits as genuine

DE TRINI=
TATIS ERRORIBVS
LIBRI SEPTEM.

Per Michaelem Serueto, aliâs
Reues ab Aragonia
Hiſpanum.

Anno M. D. XXXI

DIALOGO=
RVM DE TRINITATE
LIBRI DVO.

DE IVSTICIA REGNI CHRI.
ſti, Capitula Quatuor.

PER MICHAELEM SERVETO,
aliâs Reues, ab Aragonia
Hiſpanum.

Anno M. D. XXXII.

Faesimile of title pages of genuine original editions of the first two publications of Servetus. From the Girardot de Préfond-MacCarthy-Syston Park copy, now in the possession of L. L. Mackall. To be carefully distinguished from the spurious counterfeits.

[5] Copies of the Index were advertised as still for sale in the *Göttingische Zeitungen von gelehrten Sachen* for August 29, 1743, p. 614.

(with the assistance of his son), especially in view of his suspicious letter dated June 19, 1721, to Seelen (printed in the latter's "Selecta Litteraria," Lubecæ, 1726, p. 54) stating that he then had three copies of both the 1531 and 1532 volumes, which he had bought in Poland, where he could still get more but at a high price! Cf. Mosheim p. 309f. But in behalf of Serpilius I can state at least that he owned also the "Religio Medici, Argent, 1665."

Deschamps and G. Brunet, in their Supplement to J. C. Brunet's famous "Manuel," assure us that at the Morante sale (1872) a copy of the 1531 volume, *not* the original, was in its original binding, dated 1573, and that there was a similar edition of the 1532 book, both of which must, therefore, have been printed much earlier than J. C. Brunet intimated. This statement has hitherto proved a puzzle, to be solved only by reading in turn the various passages involved; and this could not be done conveniently.

Thus it now appears that Brunet did not confirm DeBure's inaccurate statement, or intimate that there was anything unusual about the MacCarthy counterfeit. Though he occasionally refers to Ebert, he never mentions the misprint CHHRSTUM (cf. above), which may have been present in both the MacCarthy counterfeit and the problematical Bearzi-Morante copy. The Bearzi and the Spanish Morante catalogues both record the binding of this copy as old, but neither mentions any date on it. The former describes the book simply as a "contrefaçon" (meaning doubtless the usual one) and Morante himself states positively that the book was a reprint made in Germany about the middle of the eighteenth century. So we have a right to be skeptical as to the authenticity or significance of the alleged date, 1573, in this case—especially as the same authorities seem equally sure about the 1532 book. For this very Bearzi-Morante copy of the 1532 volume is now in the Hispanic Society of America, and on examination it proves to be merely the *usual* counterfeit, such as is so often bound up with the CHHRSTUM reprint of the 1531 volume, as in the Bransby (Sotheby, 1828)—S. M. Jackson-Union Theological Seminary (New York), Jefferson Medical College and numerous other copies. However, the Hispanic Society owns also a *different counterfeit*[6] of the same

[6] Both these Hispanic Society books were described briefly in the Knaake auction catalogue (III, Nos. 971 and 972, February, 1907) and then in Hiersemann's catalogue 346, Nos. 1376 and 1377, 1907).

book, and this one has not only a flower basket and no cupid in the N on A2, but also a head in the lower half of the P on C6b, and further (which seems not to have been noticed hitherto), the title-page reads "IVSTITIA" instead of "IVSTICIA," though the latter form occurs on C6b as usual. The type is slightly different, e.g., the T on the title-page, and the paper is whiter and stronger. The fly-leaves bear notes in German referring to eighteenth-century books, and the binding (apparently German "Pappband") seems to belong to that period also. Some specialist in typography might be able to date it more definitely. The ornamented initials on A2 and C6b are in both reprints of this book wholly different from those in the original edition, though its use of abbreviations in the marginal notes is copied. The CHHRSTUM reprint of the 1531 volume attempts to copy the initial I on a2 but prints out in full the original abbreviations in the marginal notes. Probably there are *two* reprints of this volume also.

The 1546 Servetus Manuscript in Paris. It is universally admitted that the earliest printed account of the pulmonary circulation of the blood is that in Servetus's "Christianismi Restitutio," 1553, p. 169f., but it is not so generally known that the passage occurs already in the 1546 MS. (corresponding to Christ. Rest. bks. III–VII of De Trinitate Div.) bought by the Bibliothèque Nationale at the great La Vallière sale in 1784 (lot 912, for 240 livres). It had previously belonged (going backward!) to Gaignat, Hoym, and du Fay, and was described in the catalogues of their libraries as well as in De Bure's "Bibliographie Instructive" I, No. 757:1763 (cf. Allwoerden, p. 191f., and Mosheim, p. 458f.) Chereau[7] professed utter ignorance of its whereabouts, though it had been listed by Delisle, and Gordon had already printed a careful collation in the *Theological Review* for July, 1878, p. 417f. This MS. is not in the handwriting of Servetus, but it is a copy of an earlier draft of the

[7] Chereau strangely says (*Bull. de l'Acad. de Méd. de Paris*, 1879, p. 795): "Nous ne savons par qui il a été alors (La Vall., sale 1784) achété, ni dans quel cabinet il est passé. Tollin assure *l'avoir vu* . . . nous l'avons, nous, cherché en vain"—but the MS. had been duly included in Delisle's standard official Inventory as: "MS. Latin 18212. Mich. Servet, de Trinitate, XVI s. [ièc]le.—La Vall." (Bibl. de l'École des Chartes, XXXI, 546, 1871, for 1870). Previously it was known as MS. "Fonds La Vall. 162," as cited by Tollin in *Virchow's Archiv*, 1885, CI, 59, from old notes. Months ago I ordered a photograph of the circulation passage in this MS., but war conditions have hitherto delayed it.

"Christianismi Restitutio," corresponding to the pages in MS. in the Edinburgh copy of the book.

The Paris Copy of the "Christianismi Restitutio." Much has been written about the famous Bibliothèque Nationale copy of the "Christianismi Restitutio" bearing the name and notes of Colladon, yet its history is still partly obscure. It has suffered from *both* fire and moisture in the opinion of A. Laboulbène (*Revue Scientifique*, November 26, 1887), whose own books had been burned a few years before, so that he knew whereof he spoke.

The book was secured at the La Vallière sale in 1764 (lot 913) for 4121 livres, due to the insistence of the Abbé Desaulneys, Van Praet's predecessor as Keeper of Printed Books.

The Duc de La Vallière had acquired this book at the Gaignat sale in 1769 for 3800 livres, Gaignat bought it from de Cotte, who got it from the de Boze collection and de Boze received it from Dr. Richard Mead, in whose house Chas. Et. Jordan saw it in 1733. (Hist. d'un Voyage Litt., La Haye, 1735, p. 169f.) Mead still had it in 1740, but no one seems to have noted that it is already included in de Boze's own rare quarto catalogue, 1745.

The London Reprint of the "Christianismi Restitutio," 1723. It is usually assumed and simply stated as a fact that the unfinished London reprint (1723) of the "Christianismi Restitutio," was made for Mead from the original in his possession, but there seems to be no contemporary authority whatever for this view, or any proof that he owned the original before 1733, when Jordan saw it. Several years ago I carefully examined such documents on the seizure of the reprint as could be found in the London Public Record Office, but none of them referred to Mead even indirectly.

Mosheim (p. 372f.), who was greatly interested in the matter, believed that the actual printing was done by George Gallet (who had worked for the Huguetans in Lyon, and then was active as printer-publisher in Amsterdam) for Peter Palmer. I agree with Murr that Mead probably got his copies of both original and reprint *after* they had been unexpectedly seized by the London authorities on May 29, 1723, and that, just before sending the original to de Boze, he had had a transcript of the rest appended to his copy of the unfinished reprint, now in the Bibliothèque Nationale.

The Vienna Copy of the "Christianismi Restitutio" and Murr's Reprint 1790. Of the Vienna copies of the original and of Murr's reprint only a word can be said here, though I have examined them both myself. Perhaps it was the Prefect of the Imperial Library, Gottfried Freiherr von Swieten (the musical son of the learned editor of Boerhaave), who induced Count Samuel Teleki von Szek (1739–1822) to present the original to the Emperor Joseph II, in 1786, and probably he had already tried in vain to buy the La Vallière copy in 1784.

Even Menendez y Pelayo and the Heredia catalogue (IV, No. 4106) state that Murr's reprint was made in 1791, but the very small date at the foot of the last page of text reads: 1790, and this correct date is twice given in Murr's own "Adnotationes," etc. (1805, pp. 29, 63).

I have just been so fortunate as to discover in the Harvard Library ("C. 1346.10.2*") what is evidently the very transcript

* In fronte huius exempli ad dextram subscriptum legitur: *Danielis Márkos Szent-Iványi Transylvano-Hungari. Londini 1665. die 13 Maii.* Hocce exemplum idem est, de quo Samuel Crellius in limine codicis MS. olim Preussiani meminit, apud Ioh. Laur. Moshemium in hist. lat. Michaelis Serveti, pag. 204 [p. 181 of usual ed.], et in germanice 1748 pag. 344. *C. T. de Murr.*"[9]

used by Murr for his reprint. It is quarto size, bound in handsome German calf with gilt edges, and a fly-leaf bears the inscriptions: *recto,* "Summa Venerando REINHARDO[8] d.d.g. de Murr d. 9 Apr. 1808," and *verso,* "a. 1786 Biblioth. Cæsareæ illato*), e Vindobonensi exemplo, typis excuso A. 1553, in 8. secundum seriem paginarum, exactissime descriptus est hicce liber nitidissimus, et editus a possessore a. 1790 in 8 mai."

[8] "Reinhardo" was perhaps Franz Volkmar Reinhard (1753–1812), a learned and influential theologian and prolific preacher then living in Dresden. Like the original book this transcript consists of 734 pages and Errata; but there are usually twenty-six or twenty-seven full lines to a page (besides the running title and catchword) as compared with thirty-three in the original, and thirty-six in the reprint. The scribe, whoever he was, seems to have done his work very carefully, copying even the misprints in the original, and using similar abbreviations, which are, however, expanded in the reprint. Murr's printed list of Errata reproduces the list in the original edition without even allowing for the fact that the number of lines to a page is different. There is one exception: the Harvard MS. reads p. 3: res $\overline{\text{oim}}$, but this "omnium" was by mistake omitted in printing, and so this correction in the Errata applies to the reprint only. The anonymous reviewer in the *Allg. Lit. Ztg.*, November 20, 1792, noted that Murr's (p. 4, l. 3): *verbo cognationem* should be *verbo generationem,* as in his (?Göttingen) transcript. The Harvard MS. reads, *gñatioñe,* which abbreviation may have puzzled the printer. The MS. agrees with the reprint in reading (p. 67, l. 25) αρκη for αρχη, which the reviewer suggested might be a misprint in the original.

[9] The words "et editus . . . 8 mai" and signature were evidently written later than the rest, probably at the same time with the presentation inscription, 1808.

C. G. von Murr, who Reprinted the "Christianismi Restitutio." Christoph Gottlieb (Theophilus) von Murr (1733–1811) of Nuremberg was one of the last survivors of the now extinct species *Polybistor*. Of very varied learning, he wrote learnedly on every imaginable subject, was familiar with all possible languages, and corresponded with learned men in many countries, including England. He translated Fielding's "Voyage to Lisbon" into German (Altona, 1764, anon.) and Thos. Pennant's "British Zoology" into Latin. His elaborately learned "Adnotationes ad Bibliothecas Hallerianas Botanicam, Anatomicam, Chirurgicam et Medicinæ Practicæ cum Variis ad Scripta Michaelis Serveti Pertinentibus" (Erlangen, 1805, 4to) contains even a tabular "Quadrupedum Sinicorum Dispositio, methodo Linneanæ accomodata. Auct. C. T. de Murr," printed in *Chinese* characters!! But it must be added that his knowledge of medicine was learned and antiquarian rather than practical; he was not an M.D., and his own death is said to have been immediately caused by his clumsy use of a catheter on himself!

The writer who exerted the chief influence on Murr in his youth was none other than our old friend Sir Thomas Browne! "Præter alios paternæ bibliothecæ libros maxime arrisit Murrio nostro, tredecim tum annos nato, *Thomae Brownii* Pseudodoxia Epidemica, quippe quæ ipsius animum ita affeceret, ut sibi proponeret, omne quod reliquum esset vita tempus impendere vero," the preface by Joh. Ferd. Roth to the sale catalogue of Murr's books (Nuremberg, 1811, with portrait) tells us, and its No. 5036 is: "Brown, Th. Pseudodoxia Epidemica, d.i. Von den Irrthümern des gemeinen Mannes; a. d. Engl. u. Lat. durch Christian Peganium (Knorr von Rosenroth) mit Figg. (Nbg.) 1680 Pd." (*sic*!) Murr visited London in 1757 and again in 1761–62, and thus made the acquaintance of Birch (who took him to the Royal Society and the Soc. of Antiquaries), Hill, Askew, Taylor, Parsons, Wm. Hunter, Swinton, Glover, Garrick, Hogarth, and others, with several of whom he later corresponded.

Murr was a bibliophile, and he was particularly interested in Servetus. In 1784 he published an elaborate bibliographical essay on the "Christianismi Restitutio" in his Journal *Zur Kunstgeschichte* and a "Gesch. d. ber. span. Arztes Michael Serveto, in welcher Calvins schändliches Verfahren gegen denselben an Tag gelegt wird. Mit

Urkunden und einer Kupfert. gr. 8o." is listed among Murr's works, then (1805) "theils unter der Presse, theils . . . in Hs. zum Drucke bereit," but it was apparently never printed. Attention was called to Murr's Servetus collection in the second edition of his book on Nuremberg, and the titles are given in the auction catalogue issued in 1811 after his death.

Murr's chief Servetus treasure is No. 5102, in the Catalogus: "Magistri Guidonis de Cauliaco Inventarium s. Collectorium partis chirurgicalis Medicinæ s. Chirurgia. Lugd. 1537. Ldr. Titulus manu restitutus. Hoc ex. ob Mich. Serveti manum quæ ad calcem libri conspicitur, a b. Poss. magni æstimatum." I have tried in vain to trace this book.

Unknown Works by Servetus. The unique personal item just mentioned leads naturally to works by Servetus hitherto introuvable or entirely unknown. Mosheim at first categorically denied (1748, p. 73, 341) but later (1750, p. 34, cf. 27, after d'Artigny II, 103) admitted the existence of the "In Leonardum Fuchsium Apologia. Autore Michaele Villnovano, 1536," though he had noted that J. G. Schenck's "Biblia Iatrica," 1609, p. 410, had given the title. Haller's "Bibl. Med. Pract." II, 34, starred the title, thus indicating that he himself owned a copy, but Murr ("Adnot." p. 60f.) made elaborate efforts to trace it without result. Willis (p. 103 n.) found the title in the printed catalogue (III, 287 : 1870) of Dr. Williams's Library, London, but the book itself could not then be found. It has, however, since then turned up again. Gordon had it photographed in 1909, and he has located another copy elsewhere. Meanwhile Tollin had discovered extracts from it in Seb. Montuus's "Dialexeon Medicinalium," Lugd. 1537, and reprinted them in Rohlfs's *Deutsches Archv. f. Gesch. d. Medicin*, 1884, VII, 409f.

Sudhoff (whom I met at the Leipzig Book Exhibition in 1914) kindly informed me that a wholly unknown work: "M. Villanouanus, Epistolæ. Lutetiæ 1536," had recently come to light and then disappeared again in the stock of a bookseller in Leipzig. Let us hope that he will find it and turn it over to Sudhoff.

Chronology of Servetus on the Circulation of the Blood. The following notes emphasize the chief dates in connection with the well-known passage on the Circulation in the "Christianismi Restitutio."

1546. Earliest known form of the passage on the circulation by

S. Represented by the MS., not in handwriting of Servetus, now in the Bibliothèque Nationale, Paris, MS. Lat. 18212. Variants carefully printed by Alex. Gordon in *Theological Review*, July, 1878, p. 417f.

1553. "Christianismi Restitutio," printed by Balthasar Arnollet at Vienne, France. 1000 printed, but only three now known, Paris, Vienna, and Edinburgh Univ. (this copy lacks first 16 pp., replaced by transcript from the original draft). Reprinted 1723 (part only) and 1790. Various MS. transcripts of the whole book were made in the seventeenth and eighteenth centuries, apparently all 1665 or later, and from the Vienna copy.

1694. Wm. Wotton's "Reflections upon Ancient and Modern Learning," p. 230 quotes passage (C. R. Murr, pp. 170, l. 9 to l. 27 inclusive)—given to Wotton by Dr. Chas. Bernard, who knew only that he had it from a learned friend who had himself copied it from Servetus. Wotton's second ed. (cont. for first time Rich. Bentley's famous exposure of the "Epistles of Phalaris") has a P.S. to the Preface, explaining, p. XXVf., that Bernard received the passage from Abr. Hill, who copied it from the complete transcript in the possession of Bishop John Moore, who has now shown it to W., who prints further extracts. This transcript was made in Cassel (Mosheim, p. 344), was listed in Edw. Bernard's Oxford Cat. of MSS. in England and Ireland, 1697 (II, pt. I, 378, No. 9848, misprinted 6848), and is now in Cambridge University Library (Cat. MSS. III, 320 ; 1858). I examined Hill's MS. commonplace books in the British Museum without result.

1715. Jas. Douglas's Bibliogr. Anat. Spec., p. 189, and 1734, p. 104 merely quotes Wotton.

1723. London unfinished reprint of the "Christianismi Restitutio" has Circ. passage on pp. 143–4.

1728. (Not 1727) Allwoerden, p. 206f., prints, from transcripts, longer passage.

1763. De Bure's "Bibliographie Instructive," I, No. 756, reprints Circ. passage from Paris copy of book, making it well known.

1790. Murr's reprint, printed by Rau, Nuremberg, pp. 169f. on Circ.

1892–95. "Christianismi Restitutio" translated into German by Spiess (Wiesbaden, 3 vols.) the last section, Apol. to Melanchthon, left in Latin. The *1895* 2d *ed.* of Vol. I is really the same sheets, with new title, but omits a two-page "Vorwort."

A SIMPLE KEYWORD SYSTEM FOR INDEXING AND CLASSIFYING CLINICAL CASE HISTORIES AND CURRENT MEDICAL LITERATURE

By William H. Mercur, M.D., Pittsburgh, Pa.

ALL the ideas advanced in this article that have any clinical value revolve around two central factors: First, the difference existing between recollection and memory (see Diagram 1); second, the possibility of reviving, clinically, past recollections as well as past memories by utilizing a very simple keyword system (see Diagram 2).

The *raison d'être* for this paper is the author's conviction, founded upon personal, as well as practical, experience, that it is possible for almost any busy practitioner to practice clinical medicine much more intelligently and efficiently, if he will make use of the ideas here advanced. Furthermore, the author believes that if physicians who write clinical articles for the medical profession will utilize, practically, the keyword idea and the simple nomenclature and classification here advocated, they will succeed in convincing a much larger circle of readers of the truth of their statements than has hitherto been possible.

We will now discuss our first factor. Dr. Charles W. Burr, of Philadelphia, in an article on "Aphasia," which he published in *The New York Medical Journal*, May 9, 1914, defines so beautifully and simply the difference between recollection and memory that his definitions are here reproduced.

Recollections. "The bringing into consciousness of things stored in the cerebral cortex. It is a mental process, *an action.* It should never be confounded with memory."

Memory. "Memory is a physical thing, and passive, and it should never be confounded with recollection. It is the permanent effect of stimuli on brain and indeed on many other cells. Thought uses memories, but memories are not thoughts, until recollection brings them into consciousness."

The great value of our memory is founded upon the fact that our intelligence is altogether based upon our faculty of memory. Without it, we can keep no record of experience; without experience to refer to we can form no judgments. Based upon the faculty of memory, intelligence is possible, and from it all intelligent acts proceed (Nels Quevli). Hence, to be a successful and intelligent clinical practitioner, one must constantly try to learn from the study of clinical cases, but as it is possible to recall at will only a certain percentage of our former knowledge, one should also learn to appreciate the value of being able to file away case records for future reference. This obviates the necessity of learning the same thing over and over again. The value of combining our own personal experience with that of others as expressed in literature has been beautifully epitomized by Sir Wm. Osler.[1] "To study the phenomena of disease without books is to sail an uncharted sea, while to study books without patients is not to go to sea at all."

Our plan, in brief, offers to a busy physician a simple method of instantly reviving by means of keywords or strings what his past cases have taught him. That is, he has it in his power to put away in the form of a few building stones for future thought the more or less fugitive memories of the present.

Although the proposed plan is so simple in operation that almost anyone can readily understand and use it, a few brief preliminary remarks might be of interest. In the first place, it must be evident to every busy man that he is able to recall at will only a very small proportion of what he has really accomplished in the past, or of those things which he daily sees, hears, or reads. The amount of information, or knowledge, which any given individual can recall at will must, and does, vary greatly. For the purpose of our present argument, it can be stated in a general way that the average man is most fortunate if he is able to recall one-tenth of his former recollections, and that fully 99 per cent of all his memories, which he would like to recall, are not available to him in his daily work. Potentially, therefore, as far as our recollections are concerned, we are rarely more than one-tenth efficient. To most thinking people, the truth of this statement will be almost axiomatic. Those who doubt, or who desire further evidence, may be convinced if they will give a little

[1] "Books and Men," "Æquanimitas and Other Addresses," 1901.

study to Diagram 1, in which the difference between recollection and memory is graphically portrayed. Few of us realize, unless we have given the matter some thought, how completely our memories are bound up and associated with our thoughts, and, fur-

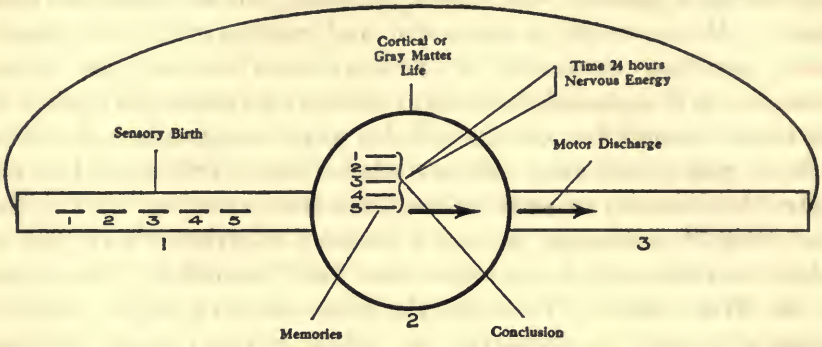


Diagram 1. Graphic Representation of the Cycle of a Normal Thought.

thermore, we do not realize that a thought on any subject, which usually flashes into our minds and out again with such marvelous rapidity, instead of being an undivided unit, can, from a mechanical standpoint, easily be divided into three distinct parts. All our sensory impressions, from which our thoughts are derived, can reach our brains in only one of two ways—first, by means of our five senses, singly or combined, and second, from memories of past sensations.

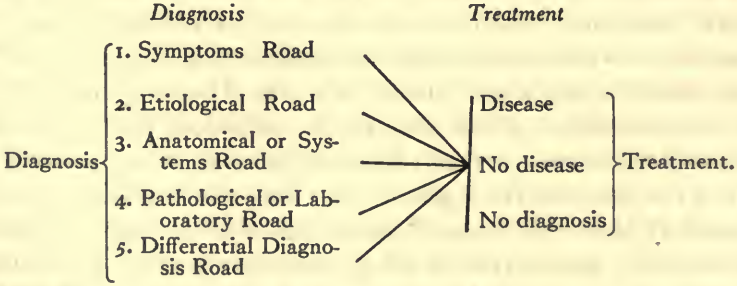


Diagram 2. Graphic Representation Keyword System.

Diagram 2 represents the course of a normal complete thought as consisting of three parts: First, a stream flowing into a lake; second, the lake into which it flows, and third, another stream as an outlet of this lake.

The stream flowing into the lake represents the sensory birth of a thought; the lake its cortical, or gray matter life; and the stream which emerges from this lake represents what occurs to a thought after being acted upon by the gray matter of the individual, and is referred to in our diagram as a motor discharge. That is, we must first arrive at a conclusion before we can translate it into some form of action. Hence, not only must all of our thoughts have a sensory birth, but nature, in order to conserve our energies, is also kind enough to index our thoughts, more or less mechanically, when they reach our brain; i.e., similar sights, sounds, tastes, etc., index or associate themselves with other previous and similar sensations.

The progress of a thought through this simple diagram can be simply illustrated, if one will imagine that he has just experienced the birth of a thought that he has never had before. Naturally this thought does not associate itself with any previous thought, so it would have to take a place by itself as thought one, illustrated in diagram as line No. 1. Later, as so frequently occurs, a similar thought will be born, and now thought two associates itself with thought one. To make our illustration a little more clear, imagine the birth of three more similar thoughts, or a total of five, which all line up together in our cortex. Now, without really wishing to think, one is practically forced to do so, in order to explain what this succession of events really means. An individual now takes a certain portion of his daily time, which can never exceed twenty-four hours, and associates it with a certain amount of his gray matter, and sooner or later reaches a conclusion indicated by a line in our diagram. The reason for arriving at a conclusion is that we may be able to translate our thought into some form of action. Our final conclusion is then discharged through the outlet of our lake. Thus the normal cycle of a thought is completed.

To illustrate further—one hears, suddenly, a dangerous sound; it at once associates itself with former dangerous sounds and one jumps. Sensory birth, cortical life, and motor discharge follow each other in logical but rapid succession. Our diagram will further enable the reader to understand that, as it is quite evident that no one can either eat or sleep for another, so also no one else can either think through, or have a motor discharge for, another. The chief difference between our memories and our recollections (Diagram 1)

is that our memories remain indexed in our cortical life, but our recollections, which indicate something we have thought through and translated into action, are represented by the dry bed of the stream of the motor discharge. Furthermore, if one considers the enormous number of sensory impressions which not only flow daily into our cortex, but have been doing so daily since our birth, it is self-evident that no one could possibly hope to arrive at any definite conclusion or have a motor discharge except for a small proportion of such impressions.

Although, usually, it is a comparatively easy matter for one to recall certain circumstances, it is always a most difficult matter to reassemble our past memories, when one has the time and the clinical case with which to utilize them.

The keyword system, here advocated, was devised, or rather grew out of, the necessity of the author's having to index and file away in a simple manner, not only his own case histories, but also to index a very large transportable reprint library, which he utilizes in his consultation practice. It was founded and evolved upon ideas which he got principally from three sources. The author wishes first of all to express his deep gratitude to, and his great admiration for, Dr. J. L. Whitney, of San Francisco, for the aid which he has given him in his little book, "List and Classifications of Diagnosis," which was prepared for the use of the University of California Hospital. Without the aid of Dr. Whitney's book this paper could not have been written. Dr. Whitney suggests a very simple plan for filing away all case histories with either an etiological or an anatomical diagnosis. Nothing that the author has ever seen could be better adapted for this purpose. As it was devised, primarily, for diagnosis only, it did not lend itself, except partially, to the filing away of recent medical literature. To overcome this difficulty, the author obtained the classification used in the Index Medicus from the editor of that periodical. In order to simplify matters, and not to have any overlapping of the keywords used in the Whitney classification, the author crossed out of the Index Medicus keyword system everything which Dr. Whitney's book covered, both etiologically and anatomically. No better illustration of the wonderful simplicity and value of Dr. Whitney's classification could be given than the fact that when this work was completed there was barely

1 per cent left of the Index Medicus classification. This now gave the author a foundation to build on in simplifying his methods of filing away case records and current medical literature, but it by no means solved the practical aspects of his problem, as the resulting keywords, although scientifically correct, were still far too numerous to be handled in a simple manner. At this time the author heard of a new scientific classification which had been recently installed in the Allegheny County Law Library, by their clever librarian, Mr. J. Oscar Emrick. His predecessor, who did not consider a catalogue necessary, and who was known far and near as the "Human Catalogue," died, leaving to Mr. Emrick a unique opportunity of devising a scientific modern catalogue for an enormous law library without being hampered by any traditions. As a basis for his work of scientific classification, he finally adopted the American Digest System. This starts out with the question, What does law do clinically for the public? The simple conclusion reached is: All that law can or does do for the public can be classified or grouped under seven basal headings. By subdividing, scientifically, these seven headings, 412 keywords work out; and under these 412 keywords anything that an attorney might want in the way of text books, references, legal decisions, or miscellaneous information may be readily found. It is a wonderful experience to consult this library and to find that in barely fifteen minutes a vast amount of information is available to the reader. The author then tried to apply the same scientific principle to clinical medicine, with the following results. He asked himself, What does clinical medicine do for the public? The answer is: A physician first clinically diagnoses, then treats, the public.

Clinical medicine, therefore, begins with diagnosis and ends, or should end, with treatment. Clinically speaking, and the suggested classification is offered purely as a clinical one, there are only five possible logical and scientific roads which a man can travel if he wishes to make a diagnosis. (Diagram 2.) The first is the Road of Symptoms. Clinical experience has demonstrated that patients rarely come to a physician for diagnosis or treatment unless they have symptoms, and if these are carefully collected and analyzed, a primary diagnosis can usually be made in about 60 per cent of cases. Frequently, however, the symptoms are too few in number, or they are too vague in character, to make a diagnosis, and the observer

now finds this road blocked. The second logical road presents itself as the etiological road, a road which permits of very few, but definite, subdivisions, such as Infectious Diseases, Diseases Due to Poisons, Animal Parasites, etc. If this second road is blocked, the third logical road is the Regional, or the Anatomical road, which has been most beautifully outlined and classified by Dr. Whitney. If, again, we find this road blocked, we can logically travel the fourth road: the Pathological, or Laboratory Road; and if by this time the above four roads do not lead us to a diagnosis, we find but one road left to use: the fifth, or Differential Diagnosis Road. By traveling any one or all of these five roads, and the author knows no others, we must logically arrive at our disease, or at No Disease, or at No Diagnosis. In any event, we must now treat the case. If a disease, we should treat it, if at all possible, etiologically; if this is not possible, it must be treated anatomically or symptomatically. If No Disease, it must be treated psychically, and if No Diagnosis, it must be treated symptomatically until a diagnosis can be made or the patient leaves us for someone who can make a diagnosis.

Now for the most practical part of this paper. After a physician has made a diagnosis of any given case, all he has to do is to index it, together with the complications associated with it, either etiologically or anatomically, following the Whitney classification. If, later, when one wishes to utilize it, it is not found alphabetically under one heading, it must be under the other. One cannot go wrong. The above covers the simple indexing of the first valuable source of our clinical knowledge—our case histories. To index, now, the memories of our second valuable source of current knowledge; first index and file them away under the name of the disease, as you will afterwards want to use them. As an illustration, assume that you had just read something new about Influenza. Under the heading Influenza, Diagnosis of, you file away for future use, under our five keywords, anything you have read, and wish later to recall, that is applicable to the Symptoms, Etiology, Anatomy, Pathology or New Laboratory Tests, or points in Differential Diagnosis, concerning Influenza. No difficulty will be found in filing away all your information under these five simple keywords or their logical subdivisions. When, later, you want to use this information, you simply pull one of these five strings. The practical clinical advantage of this plan is that it brings together, at the same place and time, all one wishes to recall about

past similar cases, and assembles for you when you wish to use it, in the form of building stones of thought, all the new ideas which might help you. When one considers the rapidity with which new ideas are constantly accumulating, it is a great advantage not to assemble these in advance of the actual case, as the newer data may, and often do, change all of our former conclusions. This is one of the especial time-saving factors of the proposed plan. Why build a house in advance of the time you are going to occupy it? Save your gray matter and economize your time.

The author feels that the reason why this simple keyword system has not been more extensively adopted is that no one thought that such a complicated and involved problem as the one we are dealing with could be solved in such a simple manner. Most of our problems are really very simple in their essence when we really understand them, but are most puzzling and complicated when we do not. It is not at all surprising that if a man thought that, in order to recall or remember certain things, he would have to classify and put them away in about a thousand different places, he should at once become discouraged and give up the problem as insoluble. But if he could be shown a simple way of putting all these thousand things away under only five simple headings, he would not likely regard his problem as being quite so hopeless.

The average man should not be too busy, if he is at all inclined to be systematic, to do all the necessary work involved in carrying the proposed plan for himself; but if he *is* too busy, or too unsystematic to do so, he can easily employ someone to do it for him, as the principles involved are so simple that they can easily be taught to almost any intelligent person.

The success of any scientific keyword system is founded, largely, upon the well-known psychological fact that when once our perceptions and ideas are welded together in our consciousness, they tend to persist and are easily recalled. The author, in order to make this simple plan practical, has combined the keywords of the Whitney Classification with those of the Index Medicus, and has had all these keywords mounted and arranged alphabetically on cards. All minor subdivisions which these few keywords do not provide may easily be added, when necessary, as the index and material grow, by merely following the etiological and anatomical subdivisions of Dr. Whitney.

PROTHYMIA: NOTE ON THE MORALE-CONCEPT IN XENOPHON'S "CYROPEDIA"[1]

By E. E. Southard, M.D., Sc.D.,

Bullard Professor of Neuropathology, Harvard Medical School; Late Major, Chemical Warfare Service, U. S. Army

Cyrus. To put enthusiasm (τὸ προθυμίαν ἐμβαλεῖν) into troops, nothing seems to work better than inspiring them with hopes.

Cambyses. Son, that would be like a hunter's calling his dogs all the time with game calls. At first they obey eagerly (προθύμως). But, if he fools them too often, they won't answer even if the game is there.

THIS passage is part of a long and well-balanced discussion on the art of war, a talk between Cyrus and his father, Cambyses, before Cyrus goes to war, in the "Cyropedia" (I, VI, 19). *Prothymia* (ἡ προθυμία) is a leading term in Xenophon for some aspects of what we have come to call morale. Several morale-making procedures of the constructive (or *prothymic*) group are acutely discussed in the "Cyropedia," often occurring in Socratic talks between the Persian paragon, Cyrus, and his generals. It cannot be denied that Xenophon himself, as the great specialist in retreat, was a master of morale. Into his Admirable Crichton, Cyrus, it is supposed that the great military philosopher contrived to insert virtually all the great qualities of generalship of Xenophon's own associates, the real younger Cyrus and the Spartan kings, Agesilaus and Clearchus, as well as of his teacher, Socrates, and of Xenophon himself. It is said that the Romans, such as Cato, Cicero, and the younger Scipio, highly valued the "Cyropedia" as a sort of military *vade mecum*. The Athenians did not like it too well, because in the Persian picture they saw all too clearly the Spartan outlines. If a history of the morale-concept were to be written (and this would be a rewarding task as compared with much that goes as ethical discussion nowadays),

[1] The Committee on Contributions to the Osler Anniversary Volume requests additions to knowledge based on research in some branch of medical or biological science. The writer hopes that his excursion into antiquity may be so regarded. The work was a by-product of study in connection with the Chemical Warfare Service, the service which, of all military branches, had primarily to deal with morale.

the "Cyropedia" would take no small part in the history of morale in antiquity.

Below I shall itemize the morale measures or *prothymic* procedures proposed by Xenophon in the "Cyropedia." But I wish to dwell a moment on the significance that underlies the terms *prothymia* and *prothymic* as used of constructive morale. Terms ending in *-thymia* have become rife in the literature of some of the mental sciences, especially in that of mental diseases, and, I believe, should come into more general use in the broader range of the literature of the moral and even the political sciences. Morale takes a prominent place in what might be called military ethics, to say nothing of the science or art of strategy. But we all now have ringing in the backs of our heads the James phrase, "moral equivalent of war"—we are all quite sure that in the coming struggle between nationalism and groupism the most gigantic hinges of fate are going to turn on morale. But what is morale? A nomenclature and algebra of discussion is lacking. Hence I suggest this ancient term *prothymia*, for some aspects of morale, heedless of whether more questions are raised than settled thereby.

As we examine below the morale suggestions of Xenophon, let us bear in mind the trend of a leading term like *prothymia*. Such current terms (e.g., in psychiatric literature) as *hyperthymia*, *hypothymia*, *cyclothymia*, *parathymia*, all refer to some quantitative or qualitative aspect of the emotional life. Any term ending in *-thymia* turns toward the emotional or affective side of the mental life, as the analogous terms ending in *-phrenia* (e.g., *schizophrenia*, *paraphrenia*) turn toward the intellect; terms ending in *-boulia* toward the will; and the long familiar terms ending in *-esthesia* toward the senses. *Prothymia*, then, for ourselves as well as for the Greeks, is a term which commits the users to a more or less definitely emotional theory of morale. The ending *-thymia* refers to *θυμός*, originally the heart, but by transference used (as we ourselves still use the term "heart") for the emotions of a man.

The term *prothymia*, then, draws us definitely away from the intellect and the senses that supply the intellect, and draws us definitely toward the emotions and the will, which we commonly account to be controlled by the emotions. Although we admit that morale might sharpen the senses (*hyperesthesia*), and increase the

rate, range, and accuracy of the intellect (a process, as one might say, of *hyperphrenia*), and still more readily increase the force and celerity of the will (a sort of *hyperboulia*), yet the use of the term *prothymia* would tend to commit us to a certain primacy of the emotions (some sort of *hyperthymia*) in all this. Do we mean that the process of morale-making is predominantly through the emotions, with the resultant morale something possibly in itself not emotional at all? Or do we mean that morale is a state of the soul in which emotion is the great ingredient? Does the emotion bound up in morale come by way of cause or in the shape of effect? Shall we use emotion to explain the origin of morale or to describe its character once established?

Re Xenophon's above passage on morale or, as you might say, on *prothymics*, Cambyses was talking with his son, Cyrus. They agreed that generalship was not all tactics—that supplies and health and physical training were indispensable too. Then the youthful Cyrus advanced that too naïve theory of morale which was bowled over by Cambyses, who continued:

> So with soldiers' hopes. If you raise false expectations too often, you will not be believed even when the hopes are well grounded. Son, you should refrain from saying what you are not perfectly sure of. *You may effect your purpose by making others your mouthpiece.* Faith in your own personal words of encouragement (*παραχέλευσις*), you must keep absolutely sacred to serve you in the greatest crises.

Thus early was raised, as I indicate by italicizing a sentence above, the question whether in the *prothymic* (morale-engendering) process one ought not to connive at the inspiration of *false* hopes through allowing subordinates to tell untruths. Cambyses and Cyrus had apparently no doubt of this.

Having considered tactics, supplies, hygiene, physical training, and morale, father and son speed on to questions of discipline and of the manifold process of out-tricking the enemy, not forgetting in the end the profit that attends obeying the gods. As for what I have called out-tricking the enemy, there is some material for morale discussion there also. Xenophon calls out-tricking the enemy *pleonexia* (*πλεονεξία*, form, *τὸ πλέον ἔχων*, having more, i.e., getting advantage), and Xenophon makes Cyrus and Cambyses

have a little tilt on whether, in order to learn to out-trick the enemy, one should not have practice in out-tricking one's friends. The decision is against the use of *pleonexic* practice on one's friends, though at the age of twenty-six or twenty-seven (which age Cyrus had now reached) it seemed safe (to Cambyses) to teach men how tricks like those used in hunting and trapping animals might be used towards men, one's enemies.

As for the more strictly *prothymic* methods of Cyrus (i.e., of Xenophon, perhaps), let us proceed to our analysis. There is an interesting passage in which mere exhortation is discounted, the value of previous training extolled, and the results of war cries and cheering told. So was the army of Cyrus filled with enthusiasm (*προθυμία*), emulation (*φιλοτιμία*), strength (*ῥώμη*), courage (*θάρρος*), good cheer (*παρακελευσμός*), self-control (*σωφροσύνη*), obedience (*πειθώ*). Courage in the form of *μένος* and eagerness to close with the enemy (*τό σπεύδειν συμμίξαι*) appeared later in the contest with the Assyrians. More war-cries from Cyrus, and the Assyrians fled (III, iii, 49–58).

Another practical *prothymic* procedure is hinted at in the suggestion (VI, ii, 33) that *we whet our minds when we whet our spears.*

The most practical, or at all events the most beautiful, procedure is naturally that of the Queen Panthea—witness that most *prothymic* speech of VI, iv, 5–7, and the kiss of her lips on the chariot-box of King Abradatas, going to his death.

Before undertaking an analysis of these various *prothymic* procedures of Xenophon, let us consider some modern conceptions of morale, or at least such deposit of wisdom as can readily be scraped from the maxim collections. Napoleon advised maneuvering about a fixed point only: we have chosen the ancient contribution of Xenophon as such a possible fixed point. How would the moderns agree with Xenophon?

Morale, according to Murray, is a moral condition, or conduct, or behavior, especially with regard to confidence, hope, zeal, submission to discipline. The relations of morale to ethics and psychology are plain, and the reference to the science of war is hardly less constant in our usage—a usage in English less than a century old and a frequent usage perhaps less than half a century old. Yet on virtually every page of a book like Marshal Foch's "Principles

of War" is some consideration or other bearing directly on morale. Hardly a commander but would now acknowledge the supremacy of morale in warfare, and the more so in the modern nationalistic warfare that followed Carnot and Napoleon. But is there a science of morale? Or, if there is not now a morale-science *in esse*, is there not one *in posse*, when the history of the Great War comes to be written and all the motives show forth in relief? Let us bear in mind a useful point of Marshal Foch himself: *That there is no science of war, but only an art!* Probably the same may prove true of the essence of war, the behavior called morale. Even if we should obtain a fixed point of discussion by a survey of ethics, psychology, and polemics, we should still have to stick to an old saying of Lepelletier de la Sarthe, *Dans la culture du moral, faites toujours marcher l'éducation du cœur avant celle de l'esprit.* Morale then belongs more to the heart than the head, and the task of a rational or scientific or methodical morale must seem as ridiculous to the soldier as a plan to use the stethoscope in a case of *Sursum Corda.*

The fixed point of maneuver in morale, let us say, then, is the heart and not the head. And by heart we shall freely mean a good deal more that lies in the thorax, and perhaps also the blood and brawn and much that passes under the name of physique. Perhaps we should not go so far as did Cabanis and say that morale is nothing but physique from a special point of view. Nor should we take too literally the grinning Voltaire with his "*le physique gouverne toujours le moral,*" much as we should like to condemn this friend of Frederick the Great for his own morale, doubtless based on his own scanty physique. Morale will be a matter of the heart more than of the head, more even of the belly and the members than of the head. Morale will stand less opposed to physique than to the psychic part of the man. These are some of the points that crowd into our minds when someone proposes a morale-science, a rationalization and formulation of the morale-problem, to the possible end of propaganda. One stands in awe of dished-up formulæ, of pumped-up morale, like the poor appealing patient with her plaint to the doctor, "Please don't try any of your psychotherapy on me!" And just as the morale-pumpers can be too *cérébral*, so can they rely too much on physique: it was an acute remark with some measure of truth that Rousseau made, "*Si le physique va trop bien, le moral se cor-*

rompt." The cultivation of morale by any extrinsic means strikes us as nigh to a species of corruption, and propaganda seems closely allied to fake.

Our difficulties with morale then are (*a*) of definition, partly intrinsic, partly (*b*) due to the recent introduction of the term into English, a term (*c*) which in French antedates nationalistic warfare in the Napoleonic sense, and which (*d*) has no corresponding Latin or Greek term by which the mutable modern usages could be controlled and at last fixed. It is unlikely that the intrinsic difficulties of the morale-concept will be resolved until we can arrive at better definitions of the concept itself. It was in a search for such definitions that I came upon the "Cyropedia."

Now, the "Cyropedia" manifestly contains much that bears on the modern morale-concept. Manifestly, also, however, the "Cyropedia" could not foresee the French Revolution and the developments of nationalistic warfare that followed. Accordingly, the list of morale measures to be found in a work of Xenophon cannot be exhaustive. I have preferred, therefore, to use Xenophon's leading term *prothymia* as a general caption for a certain group of constructive morale measures.

Following is a list of morale or *prothymic* factors occurring more or less prominently in Xenophon's "Cyropedia." I present a rough subdivision of these according to the predominance of emotional or of volitional ingredients:

PROTHYMIC FACTORS

Emotional	Volitional
Hope	Emulation (φιλοτιμία)
Enthusiasm (προθυμία)	Strength (σώμη)
Good cheer (παρακελευσμός)	Self-control (σπωφροσύνη)
Courage (θάρρος, μένος)	Obedience (πειθώ)
Woman-in-mind (episode of Panthea and Abradatas)	War-cries and singing
	Desire to grapple (τὸ σπεύδειν συμμίξαι)
	Spear-whetting

It may be asked whether the intellectual side of morale is not unduly neglected by Xenophon—a large question. More narrowly speaking, is there a degree of intellectuality in some of the morale-factors which Xenophon does enumerate—a side deliberately ignored in such a forced classification as that here made? Does not emulation imply some more or less rational object of rivalry? Do not self-control and obedience necessarily refer to the reason? If

one is a state of hope, or if, like King Abradatas, one goes to battle with the Queen Panthea's kiss on (*a*) lips, (*b*) armor, and (*c*) chariot-box, is not one by just so much a rationalist and above the brutes? Perhaps; but the point of the analysis here is not to trace the genesis of sundry mental states so much as to find those mental states whose induction makes for morale. To that end, few will doubt the value of suppressing intellect and stressing emotional and volitional states of morale, regardless of the technique of their bringing-about. The point comes out most plainly in an analysis of war-cries, which surely work more or less regardless of the degree of intelligence used in their construction.

But there is still greater and perhaps more important doubt whether some of these *prothymic* factors are not wrongly placed in the emotional or volitional columns. Of course behaviorists might regard the distinction between emotions and will itself as forced and unnecessary: that question can evidently not be answered with such limited material as we now possess. On the other hand, some believe that every act is so dependent on emotion that (for quite an opposite reason) the distinction between emotions and will has always been too sharply drawn. Without taking issue with either the behaviorists, or the emotional monists, we may still profitably preserve, on this practical level, a rough distinction between emotions and will.

In fine, the "Cyropedia" of Xenophon has at the least a large historical interest *re* morale, because Xenophon not only was a great general and specialist in the morale of retreat, but also could express in the historical novel and tract called "Cyropedia" a number of conceptions freed from the prejudice of politics. The picture was, to be sure, more Spartan than Athenian, and not especially Persian; nevertheless the Romans found the ideas of the "Cyropedia" permanently inspiring. Anything written before the French Revolution must either be very final or not at all final. The "Cyropedia" shows a little of both qualities.

Many of the morale measures of the "Cyropedia" fall under the general head of *prothymia*, a term derived from *θυμός*, the Greek word for strong feeling and passion, corresponding with the Latin, *animus*. Homer placed the origin of *θυμός* in the chest or sometimes in the midriff (of course, *θυμός*, *animus*, is sharply distinguished

from *θύμος, thymus,* or sweetbread). As was above stated, the ending, *-thymia,* is coming rapidly into psychiatric usage for qualities or degrees of emotional disorder. Plato even began the habit of *-thymia* compounds, when he distinguished *ἐπιθυμία,* appetite, from *θυμός,* spirit or passion. The *προ-* of *προθυμία* probably signifies readiness or willingness, and suggests pushing forward in space. But *θυμός* is also a term implying much activity (*θύω*—rushing, excitement, or burning). If, then, *θυμός* and its derivatives are to relate to emotions, it must be conceded that the behaviorists can claim much for their contention that emotion (like everything else psychical) reduces to behavior. Probably the "rushing, excitement, or burning" felt by the Greek, as his *θυμός* was in his chest, and hence the Homeric placement of *θυμός.* Moreover, *animus* and *spiritus* suggest the same thoracic placement of emotion. Xenophon and others use *athymia, ἀθυμία,* for want of heart, faint-heartedness, despondency.

Prothymic procedures, then, are enheartening, inspiriting measures. Despite the Socratic and intellectualizing tendency of Xenophon, his morale measures are within the domain of emotions and will. Whether they belong more amongst emotion-producing procedures or amongst volition-producing procedures is a special question that can hardly be answered before the whole big question of behaviorism gets an answer.

The tabulation of *prothymic* factors, above attempted, suggests a preliminary answer to the question whether morale measures are more emotional or more volitional. This preliminary answer is that an itemized list of such measures places more of them on the will side than on the feeling side.

Whether the morale or *prothymia,* duly produced according to Xenophon, is more of an emotional or more of a volitional state, it seems clear that the technique of the production of this *prothymic* status is a technique *via* the will. The roots of the terms that figure most prominently in Xenophon's account have reference to movement in some form (*θυμός* from *θύω,* rush: *ῥώμη, ῥώομαι,* to dart, *robur; μένος,* root MA, yearning, excitement; *σπεύδειν,* related to *speed; θάρρος,* related to *dare*). Other considerations deal with equally behavioristic matters, such as war-cries, singing, and good cheer (*παρακελευσμός*).

I think it safe to conclude, therefore, that the indications from Xenophon are that morale in his sense (or *prothymia*, if we may generalize from a favorite term of Xenophon) is in the making largely a volitional affair, an affair of behavior.

I call attention to the prominence of *behavior related with the chest* (*θυμός*, war-cries, etc.) as connected with *prothymia*. Frederick the Great in "Les Matinées Royales" (pp. 29–32) contributes a morale-engendering or *prothymic* principle that brings out this point *re* the chest: at least so I interpret a story Frederick the Great told his nephew. After telling the "dear nephew" about riveting the attention of Europe on his own skill in the art of war, he goes on to say,

> "I turned the head of all the Powers. Everyone considered himself lost, if he could not move *arms, feet, and head* in the Prussian style. All my soldiers came to think that they were *twice the men they had been before* when they saw that they were everywhere aped."

The italics are not Frederick's. Note that the soldiers of Frederick felt that they were *twice the men they had been before:* is not this largely a matter of felt chest-expansion, a feeling of thoracic lightness and power of expansion, a power of inspiration, aspiration, spirit, afflatus? But, as for the rest of Europe, all they did (in the words of the princely criminal) was to move *arms, feet, and head* in the Prussian style. They arrived at rhythmic imitations of the movements of the limbs and a perfect copy of the Prussian carriage of the head. But the Prussian still felt himself *twice the man.*

Conclusions. 1. The material in Xenophon's "Cyropedia" indicates the probable great value of a historical study of the morale-concept, a study that might enliven the ethics of the day.

2. The itemizing of morale-measures found in the "Cyropedia" indicates the probable success of a behavioristic version of a large part of morale as the Greeks saw it.

3. In particular, the roots of most of the words employed in Xenophon's morale-description are roots having to do with movement and speed (rather than with mere strength statistically taken), and having little to do with mere feelings.

4. In particular, also, many of the words indicate the thoracic seat of the motions engaged (e.g., the early localization of *θυμός*,

animus, strong feeling and passion, derived probably from *θύω*, rush) rather than a seat in the head or in the muscular system at large: i.e., morale of Xenophon's description is more a matter of heart than of brawn or of head, but "heart" gets a behavioristic accounting rather than one in terms of felt emotion.

5. The morale of Xenophon's day, or at least the morale of his account in the "Cyropedia," is plainly far from a complete story of morale in the modern sense, especially the morale developments in armies and nations subsequent to the French Revolution.

6. The term *prothymia* is indicated for the morale situation as depicted by Xenophon. This term has several advantages:

(*a*) The term is a leading term in Xenophon's list.

(*b*) The root word *θυμός* has deep-lying hints of motion in it, as well as general usage in compounds suggesting "heart" in a figurative sense; and the prefix *προ-* has suitable intimations of pushing forward in space.

(*c*) Modern psychiatry has come to use the theme *-thymia* in many compounds describing variants of emotion (e.g., *hyperthymia*, *parathymia*).

(*d*) The term *prothymia* is euphonious and readily suggests variants, e.g., *prothymic* (adjective to be used of morale procedures) and *prothymics* (substantive for the art of morale, or for our accumulation of facts concerning morale).

THE MEDICAL HISTORY OF TWO CRUSADES

By James J. Walsh, M.D., New York

PERHAPS nothing would seem more improbable, not to say quite impossible, to most of the men of our time than the idea that there could be any even far-fetched comparison between the medical history of the Great War through which the world has just passed and that of the wars of old times. Above all, it would seem as though there could be no possible medico-surgical comparison between our world war, "the crusade to make the world safe for democracy," and those earlier Crusades of the later Middle Ages some eight centuries ago, when Europe poured out her men so lavishly in order that the Holy Land might be made safe for all those who wished to seek inspiration for life there where His footsteps had hallowed earth. Yet the surprising thing is that recent developments in the history of medicine have made the medical, and strangest of all, as it must seem, the surgical history of these two periods take on much more of similarity than could possibly have been credited, only that the actual documents with the details of the story of that earlier period are now before us.

The most incredible feature of the old time Crusader history is the wonderful chapter which gives the details of the surgical development that took place at that time. Any surgery really worthy of the name is commonly supposed to be an evolution of the last generation. Before that, surgery confined itself almost entirely to emergency surgical intervention or to the saving or prolongation of life when there was otherwise no hope for the patient. Lives were occasionally saved by brilliant surgical interference, especially in the tying of large arteries, but except for amputations, expectant treatment was the rule, surgeons naturally dreading the occurrence of infections and the almost inevitably prolonged convalescence, to say nothing of the frequent fatalities which followed operations.

In complete contradiction to this idea, however, we have the surgical text book of Theodoric, who wrote down for us the details

of the surgical practice of his father, Ugo or Hugh of Lucca, as he was called, who was a surgeon on one of the Crusades and took advantage of the experience thus attained to develop surgery to a marvelous degree, along exactly the same lines that it has followed in its recent evolution. The most surprising things Theodoric tells us are with regard to the variety of the surgical operations performed by his father, and the extent to which he went in surgical intervention for the saving of life and suffering. Ugo operated for tumor and for abscess within the cranial cavity, opened the thorax for pus as well as fluid, and operated within the abdomen on a great many different conditions. He, or some of his contemporaries, performed operations for the radical cure of hernia with the patient in an exaggerated Trendelenburg position, head down on a board leaning against a wall, in order that the loops of intestines might fall away from the site of operation.

Ugo's operations within the abdomen, however, are the most interesting for us, for he insisted that whenever the intestines were wounded they must be sewed up, or else the patients would die. He seems to have invented a series of special instruments and to have elaborated a detailed technic in order to repair intestinal wounds. Whenever the wound in the intestine was large, he suggested separating the bowel into two parts and placing a hollow metal cylinder within the lumen. Over this the severed intestinal ends were brought together and sewed "with fine thread made from the intestines of animals" or "with fine silk." The metal cylinder used for the purpose, he suggested, might be obtained from the sackbut, a muscial instrument of the time, from which evidently certain parts were readily removable.[1]

Theodoric tells us that the lives of a number of patients had been saved in this way, and that the metal tube would pass out after a while, but would usually not be displaced from its position until after such agglutination of the intestinal ends had taken place as would prevent leakage from the bowels. Some generations later, dissatisfied with the use of the metal tube as an adjunct, the Brancas in Italy, father and son, proposed the use of the trachea of an animal as an adjuvant to maintain the patulousness of the intestines until such healthy healing took place as would prevent leakage. Mani-

[1] See Gurlt, "Geschichte der Chirurgie."

festly, they had experienced delays and complications in the passage of the metal tube, and they suggested that this animal tissue, the cartilage of the trachea, would be gradually absorbed, but not until it had accomplished the purpose of keeping the intestinal lumen open until safe healing had taken place. It is easy to understand that men who were doing things of this kind were quite capable of surgical intervention for other conditions within the abdomen, and that they must have been rather successful, since the record of their work remains some seven centuries later.

Of course it would have been quite impossible for surgeons to have accomplished successfully such extensive operative measures without the use of some form of antiseptic. At the beginning of the late war, it is said that over 70 per cent of the wounds received in the trenches were seriously infected. Army medical departments had anticipated aseptic rather than antiseptic surgery, and were utterly unprepared for this unlooked-for state of affairs, and so their work for a time broke down rather seriously. Then there came the development of antiseptic methods, and the situation was saved, so that only a very small percentage of those who lived to reach the base hospitals died from their wounds. The methods had to be elaborated during the war, however; but, thanks to cooperation, they were soon so perfected that a great deal of suffering and mortality was saved. The immense call made on the sympathy and intellectual resources of those who saw all the suffering that there was, had almost inevitably to meet an adequate response.

Similar conditions worked a like miracle of human resourcefulness in the Crusader times. They, too, learned the precious lesson, probably not until after many lives had been lost, that certain modes of dressing wounds saved complications and sequelæ. They found empirically that strong wine was particularly likely to be followed by prompt healing. They soaked dressings of flax or linen in this fluid, covered the wound with them, and, placing other dressings above, bound up the parts. As the strong wine evaporated after a time, they called this the "dry dressing," and Theodoric was very proud of the fact that his father used it so successfully. He boasted of his getting "union by first intention" with it, and the very expression *per primam intentionem*, is a medieval Latin

phrase which has no meaning in the modern languages when translated literally as "first intention," except what it borrows from the old Latin.

Theodoric tells that his father not only cured wounds by this means, but he made them "heal solidly as before," and succeeded in obtaining "very beautiful (*pulcherrimas*) cicatrices without any ointment." These last words are a reference to the fact that many surgeons thought it necessary to make unguent applications of various kinds in order to bring about healing, yet they really only hindered union.

It is no wonder that Theodoric understood perfectly clearly the question of the formation of pus, and expressed himself very decisively against the teaching which maintained that pus was inevitable, and that the one hope of the surgeon must be to encour age the formation of a kind of pus that would do as little harm as possible to the patient. There were evidently advocates of "laudable pus," or something of that kind, at that time, and some of the older teachers had laid down the doctrine which, unfortunately, in spite of Theodoric's explanation of his father's practice, came to be accepted as the standard teaching for centuries, even to our own time. Neuberger, the German historian of medicine, quotes Theodoric as saying: "For it is not necessary—as Roger and Roland have said, as most of their disciples teach, and as almost all *modern* (italics ours to call attention to the use of the word 'modern' in the thirteenth century) surgeons practice—to favor the generation of pus in wounds. The doctrine is a very great error. To follow such teachings is simply to put an obstacle in the way of nature's efforts, to prolong the diseased action, and to prohibit the agglutination and final consolidation of the wound."

After reading this, it is much easier to understand some of the details of this Crusader surgeon's technic, as given in his son's text book. It is summarized in Gurlt's "Geschichte der Chirurgie" (Berlin, 1898). He insisted on special care in bringing together the edges of wounds, both deep and superficial sutures being employed if necessary. He declared against the common teaching of the time as to the use of a wick of absorbent material for draining. His reason was that this prolonged healing, encouraged uncleanliness, and hampered repair and cicatrization. He warned against the use of

salves in wounds of the scalp particularly, and called attention to the possibilities of serious complications here. The hair should be shaved and a compress soaked in hot wine employed to bring the edges together, sutures being dangerous. He had seen many patients recover completely from injuries to the brain even after the loss of some brain substance, though many surgeons had declared that event surely fatal. He had seen one case where one of the cells of the brain (probably a ventricle, as Gurlt suggests) had been completely evacuated, and yet the patient recovered perfectly—an anticipation of our famous tamping-iron case. He describes in detail how tonsils should be removed, the uvula clipped, pharyngeal abscesses opened, and nasal polyps removed. He dared even to suggest radical operations for goiter, though he warned of the danger from hemorrhage, and that, therefore, the operation must be undertaken only with the greatest care and foresight.

Almost needless to say, it would have been quite impossible to have done such extensive deliberate operating as is thus suggested on head, neck, and abdomen without anesthetics. The greatest surprise of all is to find that they were using anesthetics very commonly at this time. When the English poet Middleton, early in the seventeenth century, wrote of "the pities of old surgeons who put their patients to sleep before they cut them," his readers of the generations before ours scarcely knew what to make of Middleton's suggestion of a former anticipation of what seems to us *our* anesthesia. The old Crusader surgeons, and among them particularly Ugo of Lucca, used a combination of mandragora, opium, wild lettuce, and hyoscyamus for anesthetic purposes. Tinctures of these pharmacals were employed and a sponge saturated with them. The technic of anesthesia was to allow this to dry in the sun, and then, having placed it in boiling water, to allow the patient who was to be operated on to inhale the steam from it. The use of a sponge in this way and the obtaining of narcosis by inhalation is particularly interesting. There is no doubt at all that these old surgeons thus secured thoroughly efficient anesthesia, though, almost needless to say, their anesthetics were neither so safe nor so certain nor so reliable as ours.

No wonder that surgeons who had solved the hardest surgical problems so successfully as all this indicates could give explicit

directions for the bandaging of a compound fracture as simply as possible, with a compress over the wound moistened in warm wine, the dressing not to be touched for ten days unless some complication was manifestly developing. No albumin bandage was to be used in compound fractures, and lard and honey salves must be avoided. No wonder, either, that they warn of the possibility of capillary fractures of the skull, or of fracture by *contrecoup*, that is, on the opposite side, from the blow or injury. Manifestly, they were men deeply intent on their work, making careful clinical observations and not dependent at all on theory or tradition unless it was supported by their own experience.

Such good surgery could not have been accomplished except in well-conducted, thoroughly organized, and faithfully maintained hospitals. We all know now that for good surgery, good nursing and good hospitals are absolutely indispensable co-ordinate conditions, and that before Lister's time the difficulty of doing good surgery was greatly increased, not only by the lack of knowledge of the principles of antisepsis, but also by the extremely unfortunate conditions of the hospitals of that time. The nurses were often "ten-day women," usually of no character, always looked upon as scarcely more than menials, with only the most meager knowledge of how to care for medical patients, and knowing next to nothing about the care of surgical patients.

In this, then, was the second significant anticipation of our modern developments, for quite literally they must have had good hospitals and good nurses. This is actually what is found in the medical history of the time, for the hospitals very soon after the beginning of the old Crusading period had become beautiful buildings, and the care of the patients in them was carried to a point of refinement that has made them examples in history. We have the story of the organization of a series of nursing orders, both men and women, whose one purpose was the care of wounded and ailing Crusaders. The famous nursing order of St. John of Jerusalem, whose original purpose was solely to bring in the wounded and to serve in the hospitals, and who came as a consequence to be called the Hospitallers, is a typical example.

According to the letter of a pilgrim, about the middle of the twelfth century, their hospital of St. John of Jerusalem was capable

of taking care of 2000 patients.[2] This would give one an idea of how extensive were the hospital arrangements of the time. The Ladies of St. Mary Magdalen represented the feminine branch of the Hospitallers, and their hospital, according to tradition, was scarcely less extensive. Besides, there was a nursing order of Lazarists as well as that of the Templars, whose original hospital was on the site of the Temple of Solomon, hence their name. Both the Knights of St. John and the Templars afterwards found themselves compelled to establish a fighting branch of their orders in order to defend their wounded while they were bringing them in, and to care for the pilgrims who were liable to attack. Our Red Cross met with the same dangers in our time in spite of supposed progress in humanity since. These military developments did not come, however, until well on in the thirteenth century, and in the meantime, the original purpose of a nursing order was the sole one and was fulfilled admirably.

Two things they were famous for—first, the abundance of food provided for patients, and secondly, the readiness to obtain anything for those who were suffering that could possibly do them any good. Theodoric has told us that his father considered nutrition one of the most important adjuvants for the success of the surgeon's work. He adds the weight of his own experience in this regard, and as at the time he wrote he was a man of some sixty years of age, who had had much practical experience, his opinion is of great significance. He said:

"Since, therefore, nature herself cannot bring about the manufacture of good blood without proper nutriment, nothing avails more in the healing of small as well as great wounds as the care of the nutrition of the patient. The physician must, above all, not be ignorant of the kind of food materials that generate good chyme and good blood. Out of such materials the wounded man must be fed, in order that a suitable diet shall bring about a restoration of health and the renascence of the flesh and the restoration of the continuity of the wound."

These hospitals were richly endowed, for the great heart of humanity poured itself out for these early Crusaders quite as generously as for the Crusaders of our own time. The Hospitallers of St. John of Jerusalem and the Sisters of St. Mary Magdalen came to

[2] See article, "Hospitals," Catholic Encyclopedia.

own properties in many parts of Europe. Many of these donated properties, especially along the seacoast of southern Italy, France, and Spain, came to be used as what we would call sanatoria for the care of convalescent soldiers from the wars in the East, under such circumstances as would best enable them to recover their health after the severe ills and wounds to which they had been subjected. To a great extent these houses of recuperation were in charge of the nursing sisters of St. Mary Magdalen, whose great hospital in Jerusalem was, as we have said, almost as famous as that of the Hospitallers themselves, and who took the occasion of these donations of properties to establish branch houses in many parts of the world.

By another curious anticipation of the modern time, these houses after the Crusades came to be looked upon as centers upon which calls could be made in time of flood and famine and plague and war. The development was indeed very like that of the Red Cross, and came to be a great humanitarian resource at critical times in a very wonderful way.[3]

In a word, here are rather striking anticipations in that older time of most of the developments that would, at first thought, at least, seem so surely novel in our time. There was a magnificent evolution of surgery in war time which proved of fine service for civil surgery during and after the war. Anesthesia and antisepsis were anticipated in the midst of the great needs of the time. With these, surgery developed to an almost incredible ingenuity of detail in technic and of power to save life and suffering. Hospitals had to be organized well to take care of these surgical patients, and nursing was established on a new and finely efficient footing. Through the channels of charity there flowed, quite as in our time, the offerings that made all this organization of welfare work for the Crusaders possible, and that organization carried over into the time of peace after the Crusades proved to be the best solution of the civil problems of suffering among mankind, which had before that nearly always swamped the community in which they occurred, no matter how much of good will there was.

A word in conclusion may serve to point out another similarity between the Crusading times and our own, which we have every

[3] Nutting and Dock, "History of Nursing."

right to hope will be fulfilled. A great many people have been inclined to be pessimistic as to the immediate future of civilization after the war, because so many men in the flower of their lives have been cut off by war's destructiveness that surely the next two or three generations will be seriously hampered in their efforts towards progress. The answer of a French surgeon deserves to be recalled in this regard. When it was remarked to him that France was losing an immense number of men, he said, "Oh, yes, we are losing enormously in numbers, but for every man we lose we are making two men." His idea was that it is the spirit of man and not his numerical quantity that counts for human achievement. Men who in the words of a young English poet who died during the war, "have had their souls touched by flame in the trenches," will surely have a new power to do things after they come back from the war. As one of our great captains of industry, "a dollar-a-year" man for the Government during the war, said, "What we must have now is not reconstruction, but renovation. We must not merely rebuild the old world, but renew the very face of the earth."

What happened after the medieval crusades is very interesting in this regard. Europe lost several millions of men during the twelfth century when she could apparently ill afford them from her scanty population. It might easily be expected that this would cripple the power of achievement for several centuries. As a matter of fact, it had just the opposite effect, and the crusading spirit touched the souls of men so deeply that there are not a few of us who are inclined to speak of "The Thirteenth as the Greatest of Centuries." Mere material losses do not count if only the spirit of man is aroused from over-attention to sordid, material affairs, and stimulated to do work that is significant for the mind and the heart and the soul of humanity. This deep touching of the human heart may very well prove, after our modern crusade, as after those first Crusades, to be the initiative of a magnificent period of accomplishment.

BIBLIOGRAPHY

"Cyrurgia Guidonis de Cauliaco; Cyrurgia Bruni, Teodorici Rolandi, Lanfranci, Rogerii Bertapaliæ, etc." 270 ff. folio Venetiis imp. Andreæ Torresani de Asula, 1499.

Gurlt, "Geschichte d. Chirurgie," Berlin, 1898.

Neuburger, "Geschichte d. Medizin," Stuttgart, 1908.
Buck, "The Growth of Medicine from the Earliest Times to about 1800," Yale University Press, New Haven, 1917.
Lallemand, "Histoire de la Charité," Paris, 1902–10.
Hoeser, "Geschichte christ. Krankenpflege," Berlin, 1857.
Nutting and Dock, "History of Nursing," New York, 1907.
Walsh, "The Thirteenth, Greatest of Centuries," New York, 1908.

A SOUVENIR OF THE MACARTNEY MUSEUM

By J. Collins Warren, M.D., Boston, Mass.

IN a recess of an old family cabinet there has reposed for over three-quarters of a century a portion of tanned human skin. Tradition had it that the former possessor was none other than Madame du Barry, one of the celebrities of the court of Louis XV., and that it came from the breast of that famous beauty. In one corner there is a perforation suggesting the site of the mammary nipple, which lends color to this claim. The responsibility for this story is not quite clear, but the death of the former owner of the specimen in 1867 has left this version somewhat shrouded in mystery.

On the inner surface of the specimen is a faded inscription, which with some difficulty may be deciphered as follows:

> "A portion of the skin of Madame Barré, a heroine of the French Revolution who left her body to be dissected (1810) and to be given the surgeon to defray expenses. Presented to J. M. Warren by Dr. Macartney, Professor of Trinity College, Dublin."

The young man to whom Macartney had given this specimen was one of a group of American medical students who, following the fashion of that particular period, were devoting most of their time to the Paris School. They were first and foremost pupils of Louis, or, if surgically inclined, of Dupuytren, Roux, and Civiale, but they loved to visit the great centers of medicine and surgery in Great Britain which had been the resort of their fathers at the beginning of the century. It was during one of these excursions that Dr. Warren visited Dublin, a seat of medical learning, which was beginning to attract the attention of the faculties of London and Edinburgh. No doubt it was largely due to the rising fame of James Macartney as a teacher of anatomy and surgery that the traveling student felt that he could not afford to allow such an opportunity to be neglected.

Born in Ireland in 1770, Macartney's early education was largely interfered with by the unrest of the times, but as a medical student in London he was able to pursue his studies under the many distinguished teachers who were following in the footsteps of Hunter. From the lectures of Abernethy, Cooper, Davy, Haighton, and others he was able to give his natural tastes and abilities full play. The history of his appointment as professor of anatomy and chirurgery in the University of Dublin, his struggle with the prejudices and conservatism of his colleagues, the development of the Dublin School, and the formation of his famous anatomical collection are too well told by another to permit me to dwell upon them here.[1]

At the time of the young medical student's visit to Dublin, Macartney had reached the height of his career, and in turning to the letter of the son to the father for further information about our specimen, we find incidentally much to interest us in the man himself.

"DUBLIN, AUGUST 2, 1834

"My dear Father:

". . . Part of another day I devoted to the museum of Dr. Macartney at Trinity College. He made an appointment and occupied two hours in showing me the whole of it. The preparations are many of them very fine and made by himself, he giving the greater part of his time to the sole object of preparing for his lectures on anatomy and physiology, of which he is professor in Trinity College. Among the curiosities which he has here is a paper signed by a great number of persons, himself at the head, for giving their bodies after death to be dissected. He has already the skeleton of one or two persons who have given their bodies,—one of Dr. O'Connor, whose heart he has burned. He preserves the ashes in a little bronze vase on a marble pedestal with an appropriate inscription. He also has the arm exposed with the skin on in a dried state. Besides O'Connor's body, Dr. Macartney has the skeleton of Madame Barré, a celebrated Amazon under Robespierre in the French Revolution and a correspondent of Bonaparte's. She left her body and ten pounds to have it dissected by the doctor, writing this part of her will with her own hand. He has also a portion of her skin tanned quite as good as shoe-leather, of which he gave me a piece for your museum. He has also the skeleton of a man with many of the

[1] "James Macartney, M.D., St. Andrews and Dublin, Hon. LL.D., Cambridge, F.R.S., Professor of Anatomy and Chirurgery in the University of Dublin." A Memoir by Alexander Macalister, Professor of Anatomy, Cambridge, 1900.

muscles of the back completely ossified, also of the legs, and other parts of the body. All the joints are in a state of anchylosis. The skeleton of an Irish giant seven and a half feet high is also curious.

"Dr. Macartney is one of the most eccentric men I have yet come across, and his conversation was very amusing. He seems to set but little value on his wax preparations, which he keeps in a kind of outhouse in a very good state of preservation. A small burying-ground for the remains of the dissected is just behind the dissecting room, and over the entrance a marble slab with something like the following inscription: 'Here lie the bodies of those who after their death have honorably chosen to be of use to their fellow creatures.'

"Dr. Macartney gave me some good hints as to making preparations—one for the preservation of their color, which is to immerse them, previous to putting them in spirit, in a solution of alum and nitrate of potash. Wet preparations may be injected with this for preserving their forms, and may also be sufficiently hardened to keep without the aid of spirit. . . .

"J. M. WARREN."

It will be seen at once that the written testimony is quite at variance with the version given at the beginning of this article. In order to clear up its history before giving the fragment of skin a final resting place in the museum of the Harvard Medical School, information was sought from Sir William Osler, by whom my letter was referred to Professor Alexander Macalister. In the preface to a Memoir of James Macartney, Macalister says: "When in after years it was my lot to succeed to the Professorship which he had held and when, still later, I followed his Museum from Dublin to Cambridge and taught from the specimens which his hands had made, the Macartney teaching and the Macartney traditions became to me realities of peculiar interest." I am therefore taking the liberty of giving in full a letter from Macalister to Osler.

"TORRISDALE, CAMBRIDGE,
March 20, 1916.

"As Madame du Barré (Marie Jeanne Bécu) was guillotined in Paris December 7, 1793, and was only in England for a short time in 1792 trying to sell her jewelry, it is obvious that the skeleton and story are not hers.

"The Madame Barré whose skeleton I have here was at her death an old woman over sixty, a well-known Danseuse of very bad character in

Dublin. I believe it is true that she left her body to Macartney, but I have no documentary evidence. She called herself a French woman but I believe she was Irish and really by name Barry.

"Dr. Warren is confusing two things. A certain doctor in Dublin (Dr. O'Connor) did in his will bequeath his body to Macartney and left him ten pounds to pay expenses of dissection. I have the will.

"As Barré died in poverty I think it much more likely that she died destitute and was brought in by the Resurrectionists, but there is no reference that I can remember among Macartney's papers to her. However I shall look again over them.

"P. S. There is a life of the real Comtesse du Barré, by Douglas, published in 1896, which gives particulars as to her execution and beheadal. My skeleton was not beheaded."

From the above it is quite evident that the possessor of this piece of skin was a person of the name of Barry and of Irish birth. The terminal letter "y" in the name cannot, however, be admitted as convincing evidence of nationality. In the Catalogue Général de la Bibliothèque Nationale the name is entered with various spellings, of which two will suffice.

"Du Barry. Jeanne Bécu. The authentic memoirs of the Comtesse de Barre (Du Barry) by Sir Francis N., etc.

"Mémoire Authentique de Madame la Comtesse du Barri, etc."

Under an engraving in the possession of the writer, by Humphrey, London, 1770, the title is given as Madame La Comtesse du Barrè (the "y" having been erased and replaced in ink by an "e" with a grave accent).

But we find in the catalogue referred to another person of the same name.

"Dubarry (Anne-Marie-Thérèse-Rabaudy Montressin Vve.) La cityonne condamné à mort par le tribunal révolutionaire de Toulouse au corps Législatif (pour revendiquer l'héritage de son mari)."

In view of the evidence here submitted, the claim of the king's favorite to the title of ownership may be definitely dismissed.

It is, however, quite clear that persons of the name figured in the French Revolution, and it seems highly probable that Macartney's Mrs. Barry may have masqueraded as a "cityonne Du-

barry," either carried away by revolutionary fervor as a follower of Robespierre, or serving in some capacity under Bonaparte, as a traditional foe of England. If she were sixty years old at the time of her death in 1810, she would have hardly passed her prime when her namesake was beheaded in 1793, and who knows that the possessor of this fragment of skin did not have some thrilling episode of which history tells us not?

Be that as it may, the fact remains that the old keepsake has been shorn of most of its historic prestige, and like Balzac's "La Peau de Chagrin" has been shrinking rapidly in importance. But we cannot say that this quaint old specimen has been preserved all these years wholly in vain, for has it not been resurrected to revive in memory and attract attention to the name of a surgeon and scientist who possessed that transcendent quality for a life's work —enthusiasm; one who fought hard to build up a dormant institution, and who has left behind traditions which the Dublin School should prize as among its most precious possessions?

And is not this anniversary an occasion on which our thoughts should turn to all that stands for that which is good and true, and to one who has set us an example of what a member of our profession should try to be? In this spirit I venture to seek for this tale of a bygone time a place among the contributions to the day we all delight to celebrate.

INFLUENCE OF ENGLISH MEDICINE UPON AMERICAN MEDICINE IN ITS FORMATIVE PERIOD.[1]

By William H. Welch, M.D., LL.D.

IMPORTANT as have been the impulses derived from other sources, kinship, community of language, and intercourse have combined to render the influences coming from England and Scotland the dominant ones in the development of American medicine. This statement is particularly applicable to the colonial period and the first half century of the independence of the United States.

After this formative period medicine in America assumed a more independent character. In the thirties and forties of the last century it received a great and beneficial impulse from France, as has been set forth so admirably by Osler in his charming paper on the American pupils of Louis. Still later from the seventies onward the greatest stimulus came from Germany, whither flocked a multitude of aspiring American students. This influence was marked especially by the development of pathology, bacteriology, and chemistry and by the establishment of laboratories. These later foreign influences, important as they were, were exerted upon a profession and a medical art already established which was predominantly English and Scottish in origin and character.

The meager body of medical knowledge brought from England and Scotland by Thomas Wotton and Samuel Fuller and the little band of their successors in the seventeenth century was considerably increased by immigrant physicians and returning students, by importation of books, and by correspondence in the following century. It was transmitted mainly by the apprenticeship system. That the

[1] As this paper has been written upon a steamship crossing to France, without access to books or notes, it has not been possible to insert references.

spirit of inquiry was not absent is shown by the additions to the indigenous materia medica, some of which have retained a permanent place, and by the introduction by Cotton Mather and Labdiel Boylston in Boston of the practice of inoculation against smallpox almost simultaneously with its introduction in England, but quite independently, and with a skill and success equal to that attained elsewhere. The eighteenth-century story of inoculation has much the same interest and runs much the same course in America as in England.

Before the end of the eighteenth century substantial contributions had been made to the knowledge, prevention, or treatment of the three great epidemic diseases which in succession sorely afflicted the colonies, namely smallpox by Labdiel Boylston, diphtheria by Samuel Bard, and yellow fever by Matthew Carey, William Currie, and Benjamin Rush. Samuel Bard's "Enquiry into the Nature, Cause and Cure of the Angina Suffocativa or Sore Throat Distemper," William Currie's "Historical Account of the Climates and Diseases of the United States," and Noah Webster's "Brief History of Epidemic and Pestilential Diseases," are the works of greatest permanent value to medicine published in this country before the close of the eighteenth century, although we cherish John Morgan's "Discourse upon the Institution of Medical Schools in America" as a precious document of our medical literature.

While Philadelphia was the medical center of America in the eighteenth century and later, and the names of its medical leaders—Colden, Cadwalader, Bond, Morgan, Shippen, Jones, Redmond, Rush, Wistar, Kuhn—sufficiently indicate their origin, there was no more cultivated and attractive group of medical men in the third quarter of the eighteenth century in America than that in Charleston, S. C., which has been so well pictured by Mumford. Of these Bull was a pupil of Boerhaave, and Chalmers, Moultrie, Lining, and Garden were trained in Edinburgh. These men were abreast of the knowledge of the day; some were naturalists as well as physicians, their names being perpetuated in those of plants, fellows of the Royal Society, and correspondents of Linnæus, Fothergill, and other European savants.

After the Revolution American medicine assumed a character of greater independence and reliance. Elihu Hubbard Smith, the

father of American medical journalism, established in 1797 *The Medical Repository*, which survived until four years after the foundation in 1820 of the journal now known as the *American Journal of the Medical Sciences*.

The most important channel of foreign influence is that of education, and it is fortunate that so vigorous and healthy an influence as that of the University of Edinburgh inspired the ideas of Morgan, Shippen, Bard, Hosack, and other founders of medical education in this country, who had been taught by Cullen, the Munros, Black, the Hamiltons, Gregory, the Bells, and other leaders of the Edinburgh School. These were the influences which presided over the foundation of the Medical School of the College of Philadelphia—later the University of Pennsylvania—in 1765, and that of Kings College—later Columbia University—in 1768. We should always recall with gratitude the deep interest and support and advice of Cullen and of John Fothergill and later Lettsom, the delightful Quaker physicians in London, who were the friends, counselors, and correspondents of so many American medical students and physicians in the latter part of the eighteenth century.

The rise in the nineteenth century of the many detached proprietary medical schools scattered over the land, sometimes in small country towns, is a phase in our medical history, peculiar to the United States, which we cannot contemplate with satisfaction. Acquaintance with the separate medical schools in London in the later eighteenth and early nineteenth centuries, such as the famous Great Windmill Street School, founded by William Hunter, Sheldon's Great Queen Street School, Marshal's School at Thavies' Inn, Brooks's School, the Webb Street School, the Little Dean Street School, and others frequented by American students, may have had some influence, but neither these nor the hospital schools in London were empowered to grant the doctor's degree nor the license to practice, and we must recognize the movement for separate schools as in the beginning a response to the urgent needs of the country for a rapid supply of physicians.

Objectionable as the system was in many respects, and inexcusably long as it lasted, the results were better than might have been anticipated, as defects were in a measure counterbalanced by the devotion of excellent teachers and by the native intelligence and

industry of the pupils. A unique product of these local conditions was the peripatetic professor, strikingly exemplified in the person of John Delamater.

The influence of English as distinguished from Scottish Medicine upon America was most marked in the latter part of the eighteenth and the first three decades of the nineteenth centuries. This came largely from the great London surgeons, Percival Pott and John Hunter and their successors, especially Abernethy and Sir Astley Cooper.

John Jones, who begins the line of American surgeons with his book for army surgeons entitled "Plain Remarks upon Wounds and Fractures," published just before the Revolutionary War, had been a pupil of Percival Pott. John Morgan, Richard Bayley, and William Shippen, Jr., studied under William or John Hunter. The list of American pupils of Sir Astley Cooper is a long one, and includes the names of John Collins Warren, James Jackson, Valentine Seaman, Valentine Mott, Dorsey, William Gibson, Alexander H. Stevens, John Kearny Rodgers, Edward Delafield, B. W. Dudley (also a pupil of Larrey), John Wagner, and others. Physick was almost as much a mouthpiece of the doctrines of John Hunter in America as Abernethy was in London.

As the Munros prevented the establishment of a chair of surgery in the University of Edinburgh until well into the nineteenth century, although John Bell was an excellent extramural teacher, early American surgery was derived mainly from the London group, and to this we may attribute the interest in anatomy, normal and pathological, which has characterized American surgery. We owe to a surgeon, the elder Gross, the first American treatise on morbid anatomy.

Matthew Baillie's classical work on morbid anatomy led in England, as Bichat's did in France, in the early nineteenth century to the first fruitful combination of clinical and pathological studies, culminating in Richard Bright's "Reports of Medical Cases" published in 1827. From both sources sprang the new era which now arose in America, but it was from pupils of Louis, namely Gerhard, aided by Stillé, the younger Jackson, and Shattuck, that there came America's great contribution, resting upon combined clinical and pathological investigations, of the sharp and decisive

distinction between typhus and typhoid fevers, following which Elisha Bartlett published the first modern, systematic treatise on fevers based upon the new doctrines.

Results of the remarkable development of ophthalmology in England in the early nineteenth century by the work of Saunders, Adams, Travers, Lawrence, and Mackenzie were brought to the United States by Edward Delafield, who with Rodgers founded the New York Eye and Ear Infirmary in 1820. As early as 1823 George Frick published in Baltimore the first original American treatise on the diseases of the eye.

The great reform in clinical teaching by Graves and Stokes in Dublin, transmitted to London by Robert Bentley Todd, had a marked influence in America, where Graves' "Clinical Lectures," the most famous ever published in English, had an enormous vogue at about the same period, when Sir Thomas Watson's "Practice" and C. J. B. Williams' "Principles of Medicine" were the admirable and favorite text books.

While America has not produced a Harvey, a Sydenham or a John Hunter, one can recognize readily the lineage and the features of familiar types of English physicians and surgeons in conspicuous members of the medical profession of this country.

Benjamin Rush, the greatest historical figure in American medicine, has been called with singular inappropriateness "the American Sydenham." He belongs rather to a type not congenial to English soil, the eighteenth century systematists, of whom Cullen and Brown, whose disciple he was, are the chief, as well as the last British representatives. There was much more of that objective naturalistic study of disease, unhampered by tradition and dogma, which characterized Sydenham, to be found in the works of Nathan Smith, Daniel Drake, and Jacob Bigelow. Physick, Mott, the Warrens, bear favorable comparison with their contemporaries in English surgery. Of the humanistic type and of the lineage of Mead, Garth, and Arbuthnot were Hosack and his pupil Francis, interested in letters and natural history, prominent in social life, withal excellent teachers and physicians, worthy to have inherited the gold-headed cane had Matthew Baillie sent it across the Atlantic to New York. Bartlett, the elder Jackson, Alonzo Clark, and the elder Flint belonged to the English type of sane, judicious, objective clinicians.

More picturesque and more distinctive of conditions then existing in America was the group of physicians and surgeons, of whom McDowell, Dudley, and Drake were the leaders, who lived in the early part of the nineteenth century on the frontier on or near the banks of the Ohio. While abreast in knowledge and skill with the best in contemporary medicine, they had all the indomitable pluck, the resourcefulness, and the native vigor of mind and body which characterized the pioneers who won the West.

There has been no analogy in America to the London hospital medical schools. These have their shortcomings as well as good features, but efforts to unify and to prove them do not encounter one of the main difficulties in improving medical education in America, where hospitals and medical schools originated and were developed apart from each other and the need of their affiliation or union meets serious obstacles. The admirable system of dressers and clinical clerks found in British hospitals was introduced first in America by Osler at the Johns Hopkins Hospital.

Nothing has been more remarkable during the last generation in American medicine than the establishment of independent institutions for medical research and the rapid improvement in medical education, so that our country in opportunities for the training of students and the promotion of knowledge compares favorably with those of Europe.

In these last remarks I have passed beyond the historical period set for this paper. It would transgress both this and the limits of space allowed were I to attempt to speak of the important influence upon American physiology of one of the glories of modern English medicine, its school of physiology, or of the great developments in the organization and administration of public health, in which England leads the world, although in this field America too has made valuable original contributions.

One of the results of the Great War has been to direct attention forcibly to the state of science, medicine, and public hygiene in the leading countries of the civilized world with the view of profiting by the lessons of the war and of readjustment to profoundly changed internal and international conditions. The minds of both the profession and the public have been awakened to the need of improvement in education and practice in science, medicine, and public

health, of ampler provision for advancing and applying useful knowledge, and of establishing between countries recently associated in the war closer scientific relations and better reciprocal opportunities for graduate study. Considerations such as these make it well to recall the intimate association of British medicine and American medicine in the past and to look forward to a future of mutual helpfulness in which America may be able to repay a part of her debt to British medicine.

THE EYES OF THE BURROWING OWL

WITH SPECIAL REFERENCE TO THE FUNDUS OCULI

By Casey A. Wood, M.D., Chicago, Ill.

OF all the Strigiformes there is none so interesting from the standpoint of the visual apparatus as that widely distributed New World group—the Burrowing Owls. These birds are found (as the typical species, *Speotyto cunicularia*) throughout the pampas regions of Central South America and occasionally farther south; and are well known, as a subspecies, in Florida (*Speotyto c. floridana*), the West India Islands, and on the plains and in the valleys of North America (*Speotyto c. hypogæa*) as far north as British Columbia.

Of the numerous subspecies may be mentioned also the small, pale-brown, insectivorous, Short-Winged Burrowing Owl (*Speotyto c. brachyptera*) inhabiting the island of Santa Margarita, Venezuela; and the Haitian form—*Speotyto c. dominicensis*. The Florida Owl is also seen in the Bahamas. Although smaller than the typical species, it has larger feet and bill; the plumage is, on the whole, darker, with clear white spots.

All Burrowing Owls are comparatively small (less than 11 inches in length), but this peculiarity is not so noticeable on account of their unusually long, bare legs. Their habits are said to be mainly diurnal, but observations of the North American species by the writer incline him to the belief that they are essentially nocturnal animals, like most owls. Burrowing habits seem to be common to all the species.

Burrowing owls have a dull-brownish, spotted, and barred plumage; the middle of the chest is white and is partly encircled by a plainly marked buff-brown collar. The head is rather flat and small, the facial disks are not well defined, the bill is short, and the wings are relatively undeveloped, so the bird is able to fly only short distances.

The food of these owls consists almost entirely of mice, gophers, and similar mammals, as well as of small reptiles and insects. Of these a family of owls, commonly ten in number, will consume enormous quantities; each member disposing of his own weight of pabulum in twenty-four hours!

According to Knowlton and Ridgway (1) the Burrowing Owl is more or less migratory, and after a return to its usual habitat mates (probably for life) and then arranges its underground nest. The contour of these nesting burrows varies; they are usually about 15 inches wide and from 5 to 10 feet in length. They enter the ground in a diagonal direction for a few feet and then turn at an angle either to the right or to the left. The nesting chamber (12 to 18 inches in width), placed at the highest part of the burrow, is mostly lined with dry dung, but sometimes with hair, feathers, or dried grass. The eggs are six to twelve (generally eight) in number; their color, when unsoiled, is glossy white.

It must be remembered that while the great majority of these owls dig their own burrows, many of them, especially the northern varieties, make use of the abandoned holes of certain mammals, notably of the prairie dog, fox, badger, skunk, and ground squirrel. Doubtless in the latter instances the Burrowing Owl may enlarge or otherwise alter the size, length, and other dimensions of the newly acquired hole.

The Burrowing Owl is not over-clean in his habits; the nesting chamber and the remainder of the burrow are often filthy and foul smelling.

The writer has studied the habits of the North American and Florida subspecies, with special attention to the eyes and eyesight of the bird. From these observations he concludes that this owl, like all the others, is a true night bird, adapting itself with but slight success to daylight conditions. In spite of the fact that Bendire and Hudson refer to the animal as a diurnal owl, their accounts of its habits really bear out the writer's contention of a nocturnal animal with fairly good day vision, yet distinctly embarrassed, uncertain, and confused when the eyes are exposed to bright sunlight. Stress is laid by a number of observers upon the fact that this owl is seen at all times of the day standing guard, often on a little mound of earth in front of his burrow entrance, forgetting that, as a much

more interested householder, he also watches from the same post all hours of the night!

Bendire gives the best account of their habits as observed by a daylight student of their habits:

"When not unduly molested, they are not all shy, and usually allow one to approach them near enough to note their curious antics. Their long, slender legs give them a rather comical look—a sort of top-heavy appearance. Should you circle around them they will keep you constantly in view, and if this is kept up it sometimes seems as if they were in danger of twisting their heads off in attempting to keep you in sight. *They hunt their prey mostly in the early evening and throughout the night, more rarely in the daytime.* As soon as the sun goes down they become exceedingly active and especially so during the breeding season."

As one result of a rather extensive study of the visual apparatus of this interesting owl, the writer has never seen anything to convince him that the bird ever performs an act requiring distinct diurnal vision. Certainly the northern bird is decidedly nocturnal, occasionally using his eyes, but at a disadvantage, during daylight hours.

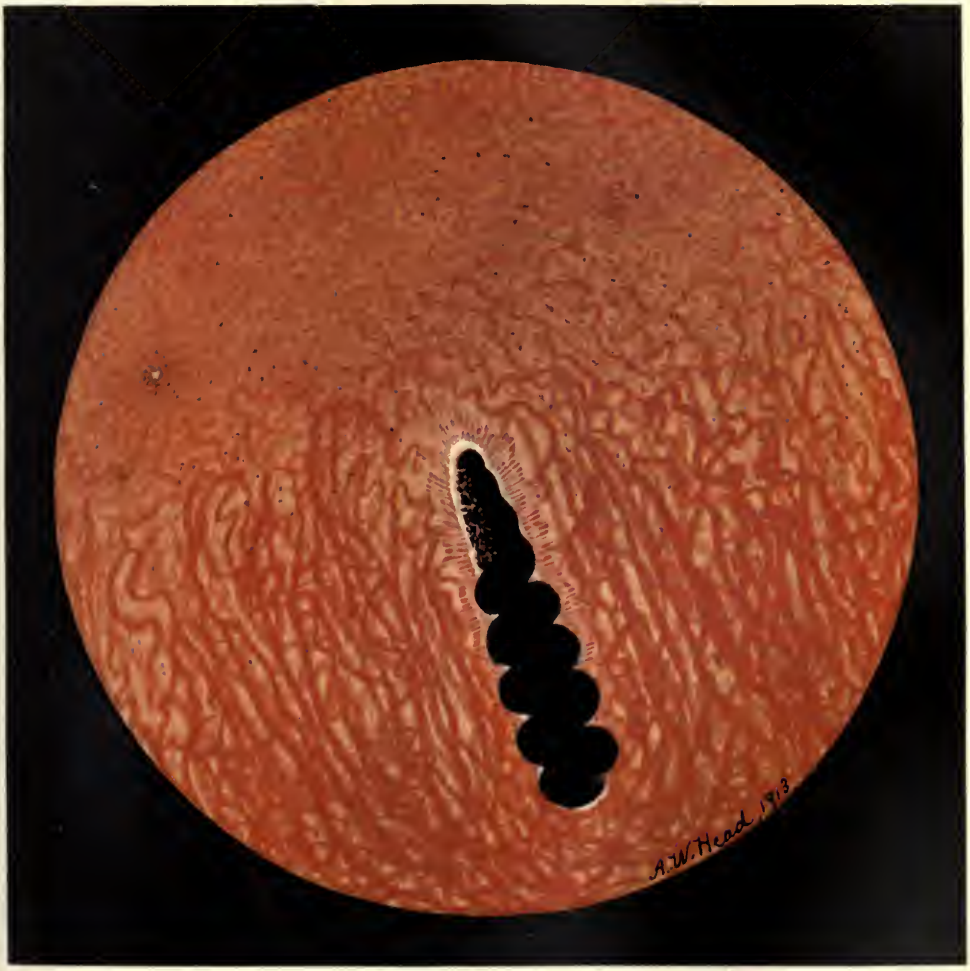
This conclusion is confirmed in a noteworthy fashion by a comparison of the fundus oculi of this owl with the same picture in owls entirely nocturnal in their habits, and indeed with certain other evidence (especially that they all show orange or reddish fundi) constantly found in night animals.

These facts have been fully stated by G. Lindsay Johnson (2) as regards the mammalia; and by the writer (3) for the avian eye.

As in all owls, the eyeballs are set well in front and surrounded by more or less plainly marked, uniform and complete facial disks (that probably act as reflectors into the eye of the diffused and faint rays of evening light).

Strigiform eyes more closely than those of any other order resemble human eyes; and they preserve, as in man, about the same relation to other facial organs and are so placed as to obtain binocular vision *in front*. Structurally, of course, birds' eyes are quite different, especially in the morphology of the eyeball, in the possession by the owl of a pecten instead of retinal vessels, in the covered optic nerve and in many other particulars which it is not proper to specify here.

Slonaker (4) and the writer (5) have pointed out that all the owls are exceptions to the rule that the retinal area of distinct vision

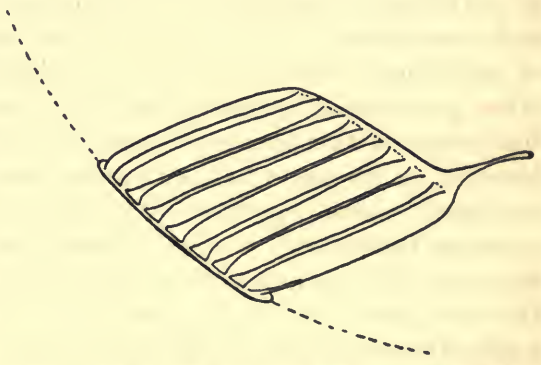


The Fundus Oculi of the Burrowing Owl—*Speotyto cunicularia hypogæa.*

is in birds with a single fovea placed above and towards the *nasal* aspect of the optic nerve entrance. The owls possess a single, deep fovea encircled by a round, sharply defined area located above and on the *temporal* side of the optic disk. This arrangement closely approaches the binocular maculæ of man.

The writer gives to the owls a class by itself in describing these areæ and affirms that the temporal *monomacular fundus* is found almost exclusively in the owls.

In conjunction with Arthur W. Head, F. Z. S., the South American Burrowing Owls in the London Zoological Gardens were closely studied and examined with the ophthalmoscope. In addition, the interior of the eyeball both of that type and of several North American individuals were examined by the writer in prepared specimens.



Lateral View of the Pecten of the Burrowing Owl—*Speotyto cunicularia hypogæa.* × 9.

The ophthalmoscope in particular shows the fundus oculi of *Speotyto cunicularia* to be that of a typical nocturnal animal. The picture of this bird's background is well shown in the accompanying colored plate, painted by Head and faithfully reproduced here. The *ocular fundus* of this species is irregularly round, as in all the owls, and in prepared specimens these details show distinctly.

The single, temporal, oval *macular region* lies above and about a disk length and a half from the upper end of the papilla. In the center of the macula is the fovea—a dark pigmented spot with fine granules arranged cap-like above it. Outside this, again, is the ovoid circumference of this region, incompletely edged with fine dots. These are more numerously distributed below the macula than above it. Connected with the macular region is a light-colored and rather broad band that extends horizontally to the center of the visible background. It is unevenly divided into two strips by a parallel arrangement of minute pigment dots.

Seen from above, the relatively small *pecten* closely resembles a disarticulated, acuminate leaf, the stem representing the spinous projection immediately above the lowest terminal convolution. The light double folds of the marsupium slope backwards and cover most of the optic entrance; they meet above in a uniform, very narrow, slightly undulating crest whose posterior end projects half the height of the underlying coil well into the vitreous cavity. An extension upwards of the long axis of the disk cuts the retinal band at the junction of the inner and second fourth, making an infulapapillary angle of, perhaps, 40°.

This interesting owl is especially subject, like other Strigiformes, to pathological variations in the fundus picture after confinement and domestication. Both Head and the writer examined a number of individuals that undoubtedly exhibited choroidal disease and other pathological changes. Rejecting these, the general color of the fundus of this species is found to be dull-orange, mottled and blotched in its upper half with deep orange-red. Choroidal vessels are plainly visible, covering all the lower part of the eyeground, just as in the Tawny Owl. The well-defined macular area is seen within the outer half of the fundus, a little above the upper extremity of the optic disk. It is distinguished from the surrounding choroid by a collection of minute pigment granules or dots with a bright, white spot in their center.

The *optic disk* is white and of oblong shape, slightly rounded at the ends. From its edges run a few short nerve fibers that form a complete fringe about the visible papilla.

The *pecten* is decidedly larger in proportion to bodily measurements than one finds it in most of the larger owls, especially larger than in the Tawny Owl. It extends well forward into the vitreous, and its lower half appears very massive and of a dark brown color. The pectinate convolutions are plainly seen and the anterior or upper half is more delicate in structure, being perforated where it joins the disk. Here it forms a dark network on the surface of the nervehead, where, also, a few red granules mingle with the chocolate-brown texture of the pecten.

BIBLIOGRAPHY

1. "Birds of the World," p. 537.
2. *Phil. Tr.*, Lond., 1901.
3. "Fundus Oculi of Birds," Chicago, 1917.
4. *Jr. Morph.*, 1897, XIII, 445.
5. *Am. Encyc. Ophth.*, 1914, IV, 2519.

THE REGULATION OF THE RED BLOOD-CELL SUPPLY

By C. H. Bunting, M.D., Madison, Wis.
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AMONG the many problems offered by the hematopoietic system, that of the regulation of the red blood-cell supply to the circulation is not the least interesting. For weeks, months, and even years of health, an individual man or animal has a peripheral red-cell count which is for all practical purposes a constant. This constant is maintained in spite of a wear and tear which results in the daily destruction of a not inconsiderable proportion of the total number of circulating red cells. Its maintenance requires the production and the supply to the circulation of an equal number of new cells daily. These new cells are produced in the erythrogenic centers within the bone-marrow and outside of the circulation. Devoid of active ameboid motion, they must pass through the endothelial lining of the vessels to enter the blood stream by means of some force developed outside of themselves—some *vis a tergo*—and in the nature of that force lies the question of the control of the red blood-cell supply. What is the impelling force which pushes enough cells into the circulation per unit of time to maintain the blood count at its level? Obviously one must seek for a mechanical cause.

One may gain a hint as to the direction in which to push his inquiry by a consideration of the rate of supply of red blood cells to the circulation. While the absolute length of life of a circulating red cell is not known, Zoja (1) and others have estimated that one-tenth of all the hemoglobin in the body is destroyed each twenty-four hours. This conclusion was reached by the determination of the amount of hemoglobin which was represented in the daily excretion of bile pigment; and it assumes that all the bile pigment is derived from hemoglobin, an assumption upon which doubt has been cast by Whipple and Hooper. (2) However, for the sake of argument, one may disregard their criticism. If one-tenth of all the hemoglobin is broken down each day, it can happen only with the destruction of

one-tenth of all the red blood cells. In other words, the life of a red cell is approximately ten days. If an adult man possesses approximately 5 liters of blood and 5,000,000 red cells per cu. mm., he must have in his circulation in the neighborhood of 25,000,000,000 red cells, and with the destruction of one-tenth of these an equal number, 2,500,000,000, must be produced each day in order to maintain his constant count. A simple mathematical operation demonstrates that if this rate of production be true the marrow must furnish to the circulation approximately 28,935,000 red cells per second of time. This rate of activity on the part of the bone marrow is almost unbelievable, yet were the length of life of the red cell fifty days, one would get the scarcely less preposterous rate of 5,787,000 cells per second as the number that must be produced to maintain the constant.

That these figures lie close to the realm of truth is indicated by figures obtained in experiments upon animals. In a series of experiments performed a number of years ago (3) in which rabbits were bled a small amount daily, I found that if the bleeding was omitted for a day the blood count would increase 500,000 cells per cu. mm. A rabbit of two kilograms in weight has approximately 100 cm. of blood, and so apparently is able (with hyperplastic marrow, it is true) to produce 50,000,000,000 red cells in twenty-four hours in addition to those lost in the daily wear and tear.

These figures suggest a continuity of action on the part of the bone marrow, and this is further indicated by the rapid response by the marrow with nucleated red cells after marrow injury. In a recent experiment a rabbit was given an intravenous dose of 4 mg. of saponin, after blood smears had been carefully searched for nucleated red cells with negative result. The experimental data are as follows:

Rabbit, albino, wt. 1545.

11:10 A.M. R.b.c. 6,476,000, W.b.c. 8000. No nucleated reds found in smear. 4 mg. saponin given in ear vein.

11:40 A.M. scattered normoblasts found.

11:58 A.M. W.b.c. 8000, 64[1] nucleated reds per cu. mm.

12:18 P.M. W.b.c. 8000, 256 nucleated reds per cu. mm.

2 P.M. W.b.c. 7500, 1045 nucleated reds per cu. mm.

[1] Number estimated from the number seen in counting 500 white cells in smear preparation.

Here we have indication of a very prompt reaction to the injury, with the appearance of a few normoblasts within one-half hour, and a large number (1045 per cu. mm.) within three hours.

In what way, it may be asked, do these figures aid in the solution of the problem of the red blood-cell supply? First, they show definitely that to deliver the number of cells, indicated as that demanded per unit of time, the marrow activity cannot be other than constant. There must be a constant outpouring of cells and not the occasional pushing of a cell into the blood stream.

In the second place, while they do not reveal absolutely the effective delivery force, they indicate, when taken in connection with marrow structure, what it must be. It is my intention to enter into a description of marrow structure at this point only so far as may be of value in elucidating the problem at hand. The marrow is an extremely labile, plastic organ enclosed in a cavity with rigid bony walls which give it fixed dimensions. This would seem to be an adaptation not without purpose. The organ itself consists of a blood-vascular system, fat cells, and the blood-forming elements supported by a reticulum, and is without white fibrous elements except in the adventitia of the arterioles. The circulation, as revealed by natural injections of the rabbit's marrow, is unlike that of any other organ, but resembles superficially that of the spleen pulp. There is no capillary net-work. Slender arterioles or arterial capillaries run from their origin near the center of the marrow, without capillary side branches or anastomoses, to the extreme periphery, where they open into wide thin-walled venous sinuses. These in turn run toward the marrow center, uniting with their adjacent fellows in pyramidal clusters, suggestive of the vascular tufts of granulation tissue, and eventually forming large collecting veins which empty into the central vein at regular intervals of about 1 mm., as shown by longitudinal marrow sections. The arterial vessels are quite thick-walled. The sinuses, on the other hand, have endothelial walls of extreme tenuity, and it must be these vessels that the blood cells enter. Between these venous sinuses are the fat-cells and the hemopoietic groups.

It is to changes in pressure relations in one of these three elements that one must look for the force which pushes the red cells into the venous sinuses. It would seem that there must be created an extra-

venous pressure which must be of quite constant nature. While the state of the fat-content of the marrow-fat cells changes, we cannot conceive of a constant activity in this element which would produce the result seen. In considering the possible rôle of the vascular system in the production of the phenomenon under consideration, one must recognize that changes in the caliber of the vessels do occur. These are in the main, however, changes that take place over a relatively long space of time and are concerned apparently with various degrees of hyperplasia of the marrow and can have nothing to do with the constant normal emigration of cells. The only vascular change that might be of importance is the regular occurrence of the pulse wave in the arterioles. They are so situated in the midst of the hematopoietic tissue between the venous sinuses that their dilatation under pulse pressure might give rise to sufficient increase in intersinus pressure to force red cells into the sinuses. Yet the repetition of that impulse would fall short of producing the same effect without one further factor which seems to me most vital. That factor lies in the hematopoietic cells themselves. The hematopoietic tissue is far from inert. Signs of cell-division, in mitotic figures, are numerous. The cells are constantly increasing in number. The birth of each cell must increase the inter-vascular tension, and to make room for it another cell must leave, and by the only available route, the blood-stream. The erythrogenic groups of cells of the marrow, as well as the leucogenic, are so arranged that the mature differentiated cells lie on the periphery of the groups, so it is these cells that would be pushed into the circulation.

It would seem, therefore, if our reasoning be true, that it is the rate of division of the erythroblastic cells which regulates the output of red cells from the marrow. Further, I think one must assume, in view of the figures given as to the marrow output, that this rate is constant and is in all probability the maximum rate for a given amount of bone marrow. In other words, in health there is a fixed *tempo* to erythrogenic tissue proliferation; and thus the number of red cells furnished the blood stream in a given time is a "function" of the amount of red marrow that a person has. The *vis a tergo* which pushes the cells into the blood stream is the increased extravascular pressure caused by division of the mother cells of the group. Each individual, therefore, apparently acquires

an amount of red marrow which at the given rate of proliferation will supply to the circulation the number of cells necessary for his daily wear and tear. That this *tempo* is the maximum rate of production seems indicated not only by the almost impossible number of cells produced, but by another finding. When an added number of cells is required in the circulation, the marrow response is not immediate. The new cells are furnished only after a delay, and only, as shown by study of the tissues, after an extension of red marrow has taken place. This extension is apparently the result of differentiation of myeloblasts into erythroblasts with the formation of new erythrogenic centers. This increase in marrow elements occurs at the expense of the adipose tissue cells which give up their fat. This possibly accounts for the lipemia noted by Boggs and Morris, (4) in experimental anemia in the rabbit. This extension of marrow is noted in all anemias, experimental and clinical, except where reaction of the marrow fails (aplastic anemia).

The stimulus to the extension of marrow seems to have been conclusively demonstrated by Dr. Loevenhart (5) and his associates to be a deficiency of oxygen. In atmospheres of diminished oxygen content there is a marrow extension which results, after an interval, in an increase in the peripheral red-cell count. This interval, when taken with the sections of the marrow (which I have been privileged to study), would indicate that the increase was not due to a change in rate of proliferation of pre-existing red marrow, but to the normal *tempo* applied to an increased amount of marrow. This is confirmed further by the fact that the count returns slowly to normal after the animal is returned to an atmosphere of normal oxygen content.

The evidence at hand, then, would seem to indicate that the constancy of the peripheral red-cell count is maintained by a maximum activity of a fixed (for normal conditions) amount of red bone-marrow, and that the active force producing emigration is the force exerted by division and growth of red-cell progenitors.

BIBLIOGRAPHY

1. Zoja, *Folia Hæmatol.*, 1910, X, 232.
2. Whipple and Hooper, *J. Exper. M.*, 1913, XVII, 593.
3. Bunting, *J. Exper. M.*, 1906, VIII, 625.
4. Boggs and Morris, *Tr. Ass. Am. Physicians*, 1909, XXIV, 467.
5. Dallwig, Kolls, Loevenhart, *Am. J. Physiol.*, 1915, XXXIX.

THE ACTION OF ADRENALIN ON THE LEUCOCYTES AND ERYTHROCYTES

A CONSIDERATION OF THE MECHANISM BY WHICH THE ACTION IS BROUGHT ABOUT

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THE symptom of marked asthenia so prominent in the recent epidemic of influenza and influenza pneumonia, together with some autopsy findings recorded in another place, (1) suggested to me the advisability of carrying out adrenalin treatment in a series of such cases, not with the idea of supporting the circulation, but of supplying a substance which we assumed was lost to a greater or less degree by the effect of the infecting agent or its toxin upon the chromaffin tissues.

While pursuing this investigation, my attention was called to the work of Hatigan (2) on the changes in the white blood cells caused by the subcutaneous injection of adrenalin. We were, at the same time, investigating the treatment of influenza pneumonia by the intravenous injection of non-specific protein (3) (typhoid protein), particularly because of the effect of the protein on the production of leucocytes. Hatigan's report led me to investigate this point with regard to adrenalin, and to trace, if possible, the relation of the leucocyte changes induced by adrenalin to those induced by typhoid protein.

Order of Investigation. Control counts were made, usually, just before and, in some instances, several times before the injection of adrenalin. After the injection, counts were made every half hour for two hours and every hour thereafter until the leucocytes returned to the numbers noted in the control or until, for other reasons, the experiment had to be terminated.[1] In Case XVII counts were made every quarter of an hour after the injection, for two hours, and every half hour thereafter. In those cases in which food was taken during the experiment, it is so noted in the records. Differential counts were made with 1/12 oil-immersion lens.

[1] Acknowledgment is due to my interne, Dr. Campbell Harvey, for his painstaking assistance in making total leucocyte counts. Each count was verified by a second count.

TABLE I

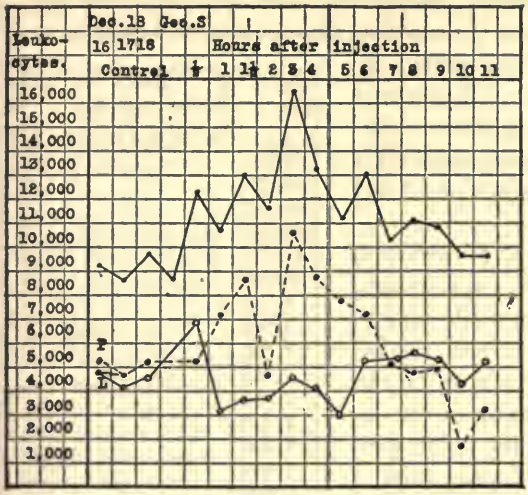
SUCCESSIVE LEUCOCYTE COUNTS FOLLOWING THE INJECTION OF 1 MG. OF ADRENALIN

No.		Control	Hours after Injection: ½	1	1½	2	3	4	5	6	7	8
1	Normal	8,700	**12,500**	10,700	13,000	11,700	16,600	13,200	11,100	13,000	10,500	11,100
2	Normal	13,900	17,900	**19,500**	14,100	13,900	17,900	16,300	14,100	12,200		
3	Normal	6,400	8,000	**8,200**	6,200	5,600	6,000		8,500			
4	Normal	6,800	**12,800**	6,900	7,200	7,300	8,900		7,600			
5	Normal	5,300	**7,500**	6,100	5,200	6,100	5,800	6,700	6,700	8,400	8,700	
6	Normal	8,050	**13,800**	6,200	7,400	8,100	9,900					
7	Normal	8,400	9,800	**16,100**	16,300	13,200	17,700	12,300	16,000	10,200		
8	Mumps	8,000	**15,200**	9,600	9,200	8,100	8,200		7,800			
9	Influenza	3,200		3,000		2,900	2,800		3,200			
10	Influenza	11,700	**23,200**	12,900	17,800	17,200	11,900		11,500			
11	Pneumonia	14,500	15,400	**17,800**	13,800	15,600	15,700	12,600		14,600	13,600	
12	Pneumonia	4,100		**5,600**		4,700	4,000	4,000	3,900		4,100	
13	Pneumonia	5,600	**11,200**	4,800	4,600							
14	Pneumonia	7,100	7,200	5,300	2,400	1,800	2,500					
15	Pneumonia	3,000	3,200	3,400	3,200	3,200	3,300	3,000		2,800		2,700

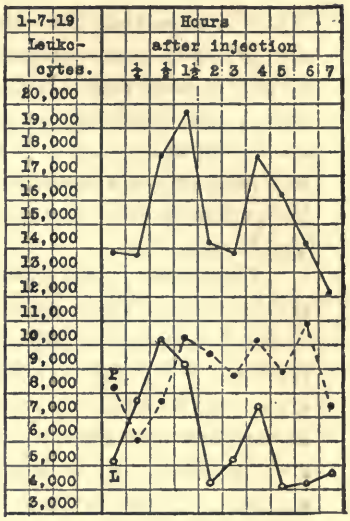
The height of the initial rise in the leucocytes is indicated by heavy type.

CASE I. TABLE II

DATE	TIME	REMARKS	LEUCOCYTES	POLYMORPHONUCLEARS	BASO. POLY.	SMALL LYMPHOCYTES	LARGE LYMPHOCYTES	TRANSITIONALS	TOTAL LYMPHOCYTES	EOSINOPHILES	ATYPICAL LYMPHOCYTES: LARGE	ATYPICAL LYMPHOCYTES: SMALL	ATYPICAL LYMPHOCYTES: SMALL RED
12-16-18	6:00 P.M.	Control	9,400	57·5		41·0			42·5		0·5		1·0
12-17-18	7:30 A.M.	Control	8,600	52·5	0·5	37·5	0·5	0·5	46·5	1·0	4·0	0·5	3·5
12-18-18	7:30	Control	9,600	53·5	1·5	37·0	1·5	1·0	46·5	1·5	1·5	2·0	2·0
	8:10		8,700										
	8:14	Adrenalin											
	8:50		12,500	42·5		40·5		0·5	55·5	2·5	4·5		9·0
	9:20		10,700	68·0	1·0	21·0	0·6		29·5	1·3	3·0	1·0	3·3
	9:50		13,000	69·0	2·0	18·0	1·0	1·0	27·0	2·0	7·0	1·6	
	10:20		11,700	40·0		21·0	3·0		30·0	1·0	4·0	2·0	
	11:20	Dinner											
	11:30		16,600	64·0	1·0	22·0	1·0	5·0	34·0	1·5	3·0	2·0	1·0
	12:20 P.M.		13,200	68·0		23·5	0·5	1·0	30·5	0·5	2·0	2·5	1·0
	1:20		11,100	71·5		24·0			27·5	1·0	2·0	0·5	1·0
	2:20		13,000	55·0		35·5	0·5	1·0	41·5	3·0	1·0	2·5	1·0
	3:20		10,500	49·5		42·5	0·5	0·5	48·5	2·5	3·5	0·0	1·5
	4:20		11,100	46·0		44·0		0·5	51·0	3·0	3·5	1·5	1·5
	5:00	Supper											
	5:20		10,800	45·0		45·0			50·0	5·0	3·0		2·0
	6:20		9,600	18·5		71·5			74·5	7·0		3·0	2·5
	7:20		9,600	43·5	0·5	44·5		0·5	54·0	2·0	6·5		



CASE I.



CASE II.

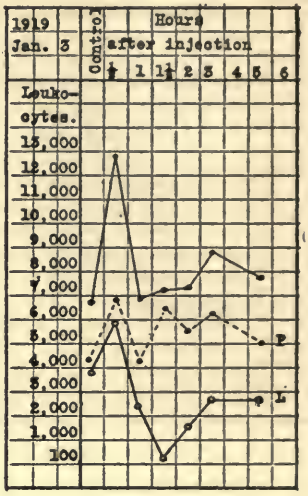
CASE II. TABLE III

Date	Time	Remarks	Leucocytes	Polymorphonuclears	Baso. Poly.	Small Lymphocytes	Large Lymphocytes	Transitionals	Total Lymphocytes	Eosinophiles	Atypical Lymphocytes: Large	Atypical Lymphocytes: Small	Atypical Lymphocytes: Small Red
1-7-19	10:35 A.M.	Control	13,900	63	1·0	32·5	0.5		35	1·5	1·5	0·5	
	10:35	Adrenalin											
	11:03		13,800	45·5	0·5	43·5		0·5	51	2·0	0·5	6·5	
	11:23		17,900	41·5	1·5	46·5	0·5	1·5	56·5	1·0	2·0	3·0	2·5
	11:53		19,500	50		36		4·0	46·5	3·5	0·5	6·0	
	12:23 P.M.		14,100	70		21		2·5	30		6·5		
	12:53		13,900	61		28·5		1·5	37·5	1·5	2·0	4·0	1·5
	1:53		17,900	55	0·5	32·5	2·5	0·5	42·5	2·0	5·0	1·5	0·5
	3:10		16,300	68·5		22·5	0·5	1·0	29	2·5	4·0	0·5	0·5
	3:53		14,100	66	0·5	24·5	0·5	0·5	31	2·5	2·5	3·0	
	4:53		12,200	61		29·5		0·5	38	1·5	5·0	2·0	0·5

CASE IV. TABLE IV

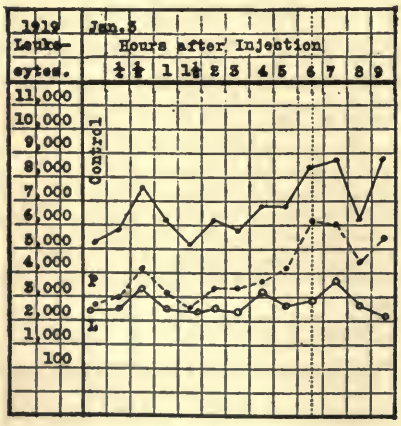
1-3-19	2:00 P.M.	Control	6,800	59·5		40·5			40·5				
	2:00	Adrenalin											
	2:30		12,800	56		25·5	0·5		46·5	1·0	6·0	0·5	10·5
	3:00		6,900	61		36·5			38·0	1·0	1·0		0·5
	3:30		7,200	81		12·5			17·5	1·5	3·0	0·5	1·5
	4:00		7,300	76		23·5			24·0			0·5	
	5:00		8,900	69·5		28·5			30·0	0·5		1·5	
	7:00		7,600	64		34·0			34·0	2·0			

All cells departing from the normal morphology were carefully observed and grouped under atypical cells. In plotting the curves, all lymphocyte forms, normal and atypical, were added together and recorded as total lymphocytes; 1 m. of adrenalin (1 c.c. 1–1000 solution P.D.) was injected intramuscularly three hours after the ingestion of food, excepting in Case XVII two hours after.



Case IV.

The Effect of Adrenalin on the Movement of the Leucocytes. In a series of 15 experiments, Table I, done on 13 individuals, made up of 5 normals, 1 mumps, 2 influenzas, and 5 influenza pneumonias, there was a rise in the leucocyte curve after the injection in 12 instances. Case IX, which did not react with an increase, was a case of influenza with a distinct leucopenia, but in this case no observation was made one-half hour after the injection; the other was a case of influenza pneumonia. In those individuals who reacted with a rise in the count, the height of the reaction was reached in half an hour after the injection in 7 instances, in an hour in 5 instances. The leucocyte increase was sustained above the control until the eighth hour in 1 (I), to the seventh in 1 (V), to the sixth in 1 (VII), to the fifth in 3 (II, III, IV), to the third in 4 (VI, VIII, X, XI), to the second in 1 (XII) and to the first hour in 1 (XIII).



Case V.

From these observations, one may conclude that an intramuscular injection of 1 mg. of adrenalin causes an increase in the leucocyte curve which reaches its height in a half to one hour after the injection, and returns to normal or to the control count in from one to nine hours. It will be further observed that a very characteristic occurrence is an initial rise and decline occupying a half to 1½ hours, subsequently followed by a second rise which is often as high as and sometimes higher than the initial rise. There is no difference in the reaction *when it occurs* in normal influenza or pneumonia cases.

CASE V. TABLE V

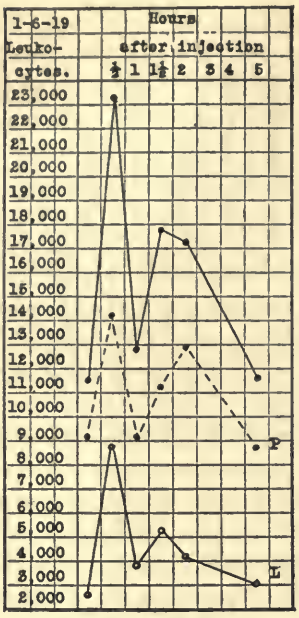
Date	Time	Remarks	Leucocytes	Polymorphonuclears	Baso. Poly.	Small Lymphocytes	Large Lymphocytes	Transitionals	Total Lymphocytes	Eosinophiles	Atypical Lymphocytes: Large	Atypical Lymphocytes: Small	Atypical Lymphocytes: Small Acidophile
1-3-19	7:40 P.M.	Control	5,300	46·5	1·0	40.5	1.0	2.0	51	1·5	4·5	2·0	1·0
	7:56	Adrenalin											
	8:12		5,800	47·8	0·4	34·3	0·4	0·4	49·5	2·3	7·9	3·7	2·8
	8:30		7,500	30·0		34·0		1·0	46·0	4·0	1·0	3·0	7·0
	8:56		6,100	52·5	2·0	33·0	0·5	1·0	44·5	1·0	1·0	6·5	2·5
	9:26		5,200	49·0		36·0	1·0	1·0	50·0	1·0	7·0	3·0	2·0
	9:56		6,100	53·0		34·5	1·0	0·5	45·5	1·0		6·5	3·0
	10:56		5,800	54·0		35·0		2·0	46·0			8·0	1·0
	11:56		6,700	45·0		46·0	2·0	1·0	51·0		1·0	1·0	
	12:00	Cup milk											
	12:56 A.M.		6,700	60·0		40·0			40·0				
	1:56		8,400	65·0		25·5	1·0	1·5	34·0	1·0	0·5	4·5	1·0
	2:20		7,100	59·0		38·0			40·0	1·0		2·0	
	3:00	Orange											
	3:56		8,700	56·0		40·0	1·0		42·0	2·0		1·0	
	4:30	Supper											
	5:56		6,300	56·0		39·0	0·5	0·5	42·5	1·5		2·5	
	6:50		8,900	60·5		34·5		0·5	37·5	1·5	0·5	2·0	

CASE IX. INFLUENZA. TABLE VI

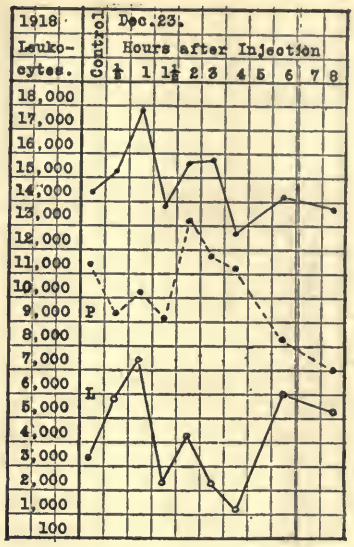
Date	Time	Remarks	Leucocytes	Polymorphonuclears	Baso. Poly.	Small Lymphocytes	Large Lymphocytes	Transitionals	Total Lymphocytes	Eosinophiles	Atypical Lymphocytes: Large	Atypical Lymphocytes: Small	Atypical Lymphocytes: Small Acidophile
2-26-18	9:00 A.M.	Control Adrenalin	3,200	73·0		27·0			27·0				
	10:00		3,000	60·5		38·0			39·0			1·0	
	11:00		2,900	69·5		30·0			30·0	0·5			
	12:00		2,800	62·0		37·0			37·0	1·0			
	1:00 P.M.		3,200	44·0		56·0			56·0				

CASE X. INFLUENZA. TABLE VII

1-6-19	Hour After inj.	Control Adrenalin	11,700	77·0		23·0			23·0				
	½		23,200	62·0	6·0	29·0			38·0	1·0		2·0	
	1		12,900	78·0		22·0			22·0				
	1½		17,800	69·0		31·0			31·0				
	2		17,200	75·0		22·0			25·0			3·0	
	5		11,500	72·0		26·0			26·0				



CASE X.



CASE XI.

CASE XI. PNEUMONIA. TABLE VIII

DATE	TIME	REMARKS	LEUCOCYTES	POLYMORPHONUCLEARS	BASO. POLY.	SMALL LYMPHOCYTES	LARGE LYMPHOCYTES	TRANSITIONALS	TOTAL LYMPHOCYTES	EOSINOPHILES	AYTIPICAL LYMPHOCYTES		
											LARGE	SMALL	SMALL ACIDOPHILE
12– –18	8:30 A.M.	Control	14,500	79·0					21				
	9:00	Adrenalin		73·0	1.0	14·5	5·5	1·0	26		4·5	0·5	
	9:30		15,400	62·0		34·5			38		0·5	0·5	2·5
	10:00		17,800	57·0		43·0			43				
	10:30		13,800	66·5	1.0	20·5	5·0		32·5		2·5		4·5
	11:00		15,600	84·0		16·0			16				
	12:00		15,700	74·0		14·5	1·5	0·5	25		5·5	2·0	1·0
	1:00 P.M.		12,600	88·5		11·0			11·5		0·5		
	3:00		14,100	57·0		38·0			43			1·0	4·0
	5:00		13,600	61·0		35·0			39		1·0	3·0	

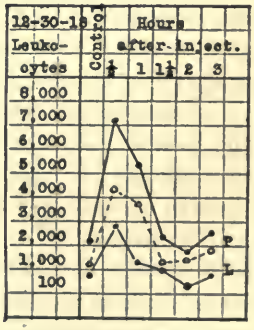
CASE XII. PNEUMONIA. TABLE IX

12–24–18	9:00 A.M.	Control Adrenalin	4,100	smear lost									
	10:00		5,600	73		27			28		1·0		
	11:00		4,700	52		48			48				
	12:00		4,000	79		7	1·0		13·8		5·0		0·8
	1:00 P.M.		4,000	76		24			24				
	3:00		3,900	52		48			48				
	5:00		4,100	35		65			65				

CASE XIV. PNEUMONIA. TABLE X

Date	Time	Remarks	Leucocytes	Polymorphonuclears	Baso. Poly.	Small Lymphocytes	Large Lymphocytes	Transitionals	Total Lymphocytes	Eosinophiles	Atypical Lymphocytes: Large	Atypical Lymphocytes: Small	Atypical Lymphocytes: Small Acidophile
12–30–18	8:15 A.M.	Control	2,100	58·0		42·0			42·0				
	2:00 P.M.	Adrenalin											
	2:30		7,200	59·0		39·0	1·0		40·0				1·0
	3:00		5,300	71·0		25·0	1·0		28·0		2·0		1·0
	3:30		2,400	57·0		41·0	1·0	1·0	42·0				
	4:00		1,800	74·0		21·0	5·0		21·0				
	5:00		2,500	69·0		27·0	3·0		28·0		1·0		

The Degree of Leucocytosis. The increase in the total leucocyte count varied between 1500 and 11,500, the average being 5000. In Case I the most marked rise came at the third hour. The count was made immediately after dinner, and, for that reason, we have not included it in the above figures. The leucocyte increases are all outside the range of experimental error, and can be justly attributed to the action of the adrenalin. The average increase in the controls is 4500, in the pneumonias 3500. The greatest increase observed, 11,500, was in an influenza case. It will be seen that no increase in the leucocytes was induced by adrenalin in one of the influenza cases and in one of the pneumonia cases, but in neither of these was an observation made during the first half hour. In all others there was an increase.



CASE XIV.

The Differential Counts. In nine of the series just recorded, differential counts were made and have been arranged in the accompanying tables and charts.

The Effect on the Polymorphonuclears. Following the injection of adrenalin, there was an initial decrease in the polymorphonuclears in 2 cases (II and XI). This decrease came within the first half hour in one case, a quarter of an hour in the other. In each case there was a subsequent rise in the polymorphonuclears, considerably above the control, 1½ to two hours after the injection. One of these cases was a normal and the other a pneumonia. There was an initial increase in the polymorphonuclears in 4 cases (IV, V, X, XIV) during the first half hour. No counts were made at this time in Cases IX and X. There was no change during the first half hour in Case I, but a marked rise occurred in

this case, at one and at 1½ hours after the injection. After the initial rise there was a sudden drop in the polymorphonuclear curve, followed by a secondary rise in four cases (I, IV, V, X). This secondary rise reaches its height at the second or third hour in all cases excepting Case V, in which it was delayed until the sixth hour. In those cases which were not characterized by an initial rise in the polymorphonuclears (I, II, XI) the subsequent rise above the control came at, practically, the same time as the secondary rise in the first group. There is also a rise at this time in Case XII, in which the control differential was not made. There was, evidently, an initial rise in the polymorphonuclears in this case.

The Effect on the Lymphocytes or Mononucleated Cells. There is an initial increase in the lymphocytes in 6 cases (I, II, IV, V, X, XI) within one-half hour after the injection of adrenalin. Even in Case IX this tendency of the lymphocytes to increase immediately after the injection is shown. This initial increase in the lymphocytes is coincident with an increase in the polymorphonuclears in 3 of these cases (IV, V, X). With the exception of Case X the increase is relative; in this case the lymphocyte increase exceeds that of the polymorphonuclears. In 3 cases (I, II, XI) the initial lymphocyte increase is coincident with a declining or stationary polymorphonuclear curve. The increase in the lymphocytes is followed by a fall as abrupt as was observed in the rise. This is often far below the control count. The fall is usually observed from one to 1½ hours after the injection. A secondary rise always takes place later on, returning to the control count in from four to five hours. In one instance, a reversal is shown in the differential curves at this time (Case I).

Acidophile Granular[2] *Lymphocyte Forms.* A careful account was made of the number of lymphocytes showing acidophile granules or particles in the protoplasm. Dr. Calhoun (4) and I have called attention to the increased number of these cells following the intravenous injection of typhoid protein in arthritis and other infections. It is of interest to note that of the 9 cases of this series in which systematic differential counts were made, there was an increase in the number of this lymphocyte form in 6. The 3 in which none of these cells was encountered were 2 influenzas and 1 pneumonia (IX, X, XII). In 2 of these there was practically no leucocytic response. In Case XIV only a few of these cells appeared after the injection, but none were found before the injection.[3] In only 1 of the other 6 cases were they found in the control in the same percentage, 1 per cent. The increase

[2] It is not at all improbable that these are azure granules or particles.

[3] It is interesting to note that two days later, at which time this patient was given an intravenous injection of typhoid protein, this acidophile small lymphocyte appeared in large numbers in the control, 16 per cent, and increased to 26 per cent one hour after the injection. This was the second day of her pneumonia.

varied from 1 to 10 per cent, average 5 per cent. These cells appear in the greatest numbers one-half hour after the injection, and disappear or return to the per cent found in the control in from one to four hours. For the most part, the cases showing the acidophile particles were the larger type of small lymphocytes with pale protoplasm. They are, however, also encountered in the small lymphocyte in which the protoplasm forms only a narrow band about the nucleus.

The Eosinophiles. Eosinophiles were increased over the control counts in 3 of the normal cases. In Case I, 1.5 per cent was observed in the control. At the ninth hour 5 per cent, at the tenth hour 7 per cent, one hour and twenty minutes after supper. Case V, control, 2.5 per cent, half an hour after the injection 4 per cent. Case II, control, 1.5 per cent, one hour after injection 3.5 per cent. There was, practically, an absence of eosinophile cells before and after the injection in the influenza and the pneumonia cases.

When one looks at the tables recording the differential counts, one is impressed with the simplicity of the blood picture induced by the adrenalin in the influenza and pneumonia cases as compared with the others, excepting in Case XI, where most of the cell forms are represented.

Discussion. Hatigan[4] (1917) observed a leucocytosis following the subcutaneous injection of 1 mg. of adrenalin. He found in the first hour after the injection that the lymphocytes were markedly increased and that they decreased the second hour, during which time the neutrophile leucocytes increased. He further observed that it usually took six hours for the number of leucocytes to return to normal, and that, if a double dose were given, the return to normal was proportionately delayed. Previous to Hatigan's observations, Castren (5) (1916) made, practically, the same observation, a marked increase in the lymphocytes and a less pronounced increase in the neutrophile leucocytes one-half hour after the injection of 1 mg. adrenalin. He states that a somewhat similar result follows muscular exercise.

The present investigation confirms the work of Castren and Hatigan in that it shows the great tendency of the lymphocytes to increase after the injection of adrenalin. It further shows that this increase is not always accompanied by a decrease in the polymorphonuclears. The lymphocyte increase is frequently coincident with

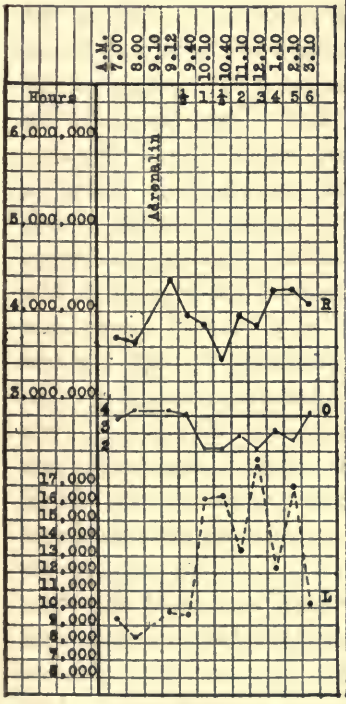
[4] Because of war conditions it was not possible to secure the original articles of Hatigan and Castren.

an increase in the polymorphonuclears, and at such a time the increase is usually purely relative. When the increase in the lymphocytes is coincident with a decline in the polymorphonuclear curve, there is an absolute and, sometimes, marked increase in the lymphocytes. This increase is greater than the loss in the neutrophile leucocytes. The neutrophile leucocyte curve almost invariably exhibits a primary and secondary rise. The secondary rise usually begins between the first and second hour, and reaches its height at the third hour.

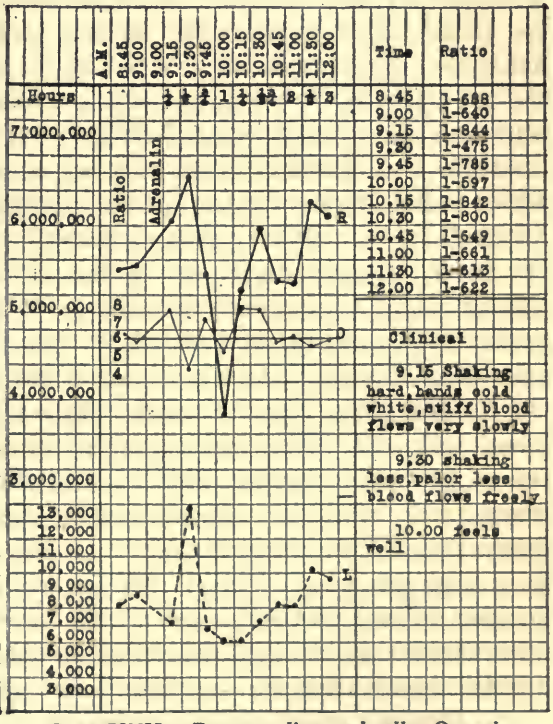
The acidophile lymphocyte is, unquestionably, increased in numbers following the injection of adrenalin. There seems to be no definite relationship between its presence and that of the eosinophile. When the eosinophile cells are encountered in the control or after adrenalin, the acidophile lymphocyte is always present, but it is also found in cases in which no eosinophiles are found. When the eosinophile lymphocyte is present in large percentages, the eosinophiles are occasionally also present—in Case I, 9 and 7 per cent respectively, in Case V, 7 and 4 per cent respectively. On the other hand, the highest acidophile lymphocyte count, 10 per cent, is encountered in Case IV, where the highest eosinophile count is 2 per cent. The significance of this cell has not yet been determined. We (4) have expressed an opinion that they are due either to some degenerative process or that they are present in response to some toxic substance.

The Effect of the Adrenalin on the Movement of the Erythrocytes. Two individuals were chosen to determine the effect of adrenalin on the red blood cells, a child and an adult; 1 mg. was injected intramuscularly. In the child, Case XVI, the counts were made every half hour until the second hour and every hour thereafter until the sixth hour. In the adult, Case XVII, the counts were made every fifteen minutes until the second hour and every half hour thereafter until the third hour. Leucocyte counts were also made. While the same general changes are observed in each experiment (see Charts XVI and XVII) more are shown when the counts are made at fifteen-minute intervals. Two control counts precede the injection in each experiment. In Case XVII there is an abrupt rise in the red-cell curve fifteen minutes after the injection. This rise reaches its height, an increase of 944,000 cells, thirty minutes after

the injection. Then comes a sudden fall. In fifteen minutes the count has returned to normal, but its downward excursion does not stop there; it continues down, and in fifteen minutes more it has reached a point far below normal, 3,704,000. This entire initial phase has occupied only one hour. The curve now ascends abruptly to near normal, which point is reached in fifteen minutes.



CASE XVI.



CASE XVII. R, upper line, red cells; O, ratio between reds and whites; L, leucocytes.

A secondary rise above normal takes place in another fifteen minutes, 1½ hours from the time of the injection, and at 2½ hours it has reached a point 800,000 cells above the control.

From these observations we may conclude that an intramuscular injection of 1 mg. of adrenalin induces an abrupt rise in the erythrocytes which lasts half an hour and is followed by a secondary rise which begins 1½ hours after the injection and continues as long as six hours. The initial rise begins very promptly, as early as two minutes after the injection.

The Mechanism by which These Blood Changes are Brought about. Changes in the number of the red and white blood corpuscles per volume of blood may be brought about experimentally in two ways: (1) By methods known to be purely mechanical; (2) by methods which stimulate increased cell production.

1. *Mechanical Methods.* The simplest of these is the local change produced by the elevation of an extremity which may lower the red blood count in the finger or toe very perceptibly. Oliver (6) has shown that the elevation of the leg for fifteen minutes may lower the red count in the toe 14 per cent and increase it in the finger 3 per cent over the control count. Extraction of water from the body by sweating and diarrhea raises the red count, as do many diseases which induce these two conditions (phthisis and cholera). John K. Mitchell (7) was the first to show the effect of massage on the blood. He noted an immediate rise in the red cells following massage. Ekgren found a temporary increase in the leucocytes, chiefly in the polymorphonuclears, from 1000 to 7000. In a case of pernicious anemia in Professor Dock's service in this hospital in 1898 I made the following observations on the effect of general massage on the blood cells and on the percentage of hemoglobin. Table XI. This report has some interest here in that the counts were made not immediately after the massage, but as late as 2¾ hours after. In 18 observations it will be seen that an increase in the red cells occurred in a large per cent of them. The increase varied from 100,000 to 400,000 as late as the second hour.[5] Excepting in one of the four observations no effect was observed on the leucocytes as late as one and two hours after the injection.

2. *Methods which Stimulate Increased Cell Production.* It has been shown (4) that the intravenous injection of foreign protein causes an increase in all members of the white cell group and also the appearance of abnormal cell forms, nucleated reds, and myelocytes. We have attributed these changes to increased histogenesis.

Roth, (9) reviewing and repeating the work of Binz, Wilkinson, Maurel, and Askenstedt, on the effect of quinine on the leucocytes, has shown that after ingestion or subcutaneous injection of quinine in animals there is a preliminary increase in the number of leucocytes in the first half hour. At this time there is a relative and an

[5] Increases below 100,000 might be within the range of experimental error.

absolute increase in the lymphocytes. This stage is followed by a leucopenia which lasts for several hours, when a secondary leucocytosis takes place, made up chiefly of polymorphonuclear cells. The same reaction was noted in man, but to a less marked degree.

TABLE XI

EFFECT OF MASSAGE ON THE RED BLOOD CELLS

DATE, 1898	RED CELLS BEFORE MASSAGE	RED CELLS AFTER MASSAGE	HEMOGLOBIN		TIME AFTER MASSAGE HR. MIN.	TIME MASSAGE GIVEN MIN.	INCREASE IN RED CELLS	LEUCOCYTES	
			B*	A*				BEFORE	AFTER
1–29	1,164,800	1,176,000	30	30	1 00	45	11,200	4,838	14,006
1–30	1,262,400	1,472,000	30	35	2 00	30	209,600	7,639	6,621
2– 2	1,267,200	1,292,800	30	30	2 45	15	35,600	5,602	7,385
2– 3	1,325,600	1,313,600	30	30	2 35	30			6,780
2– 5	1,233,750	1,408,000	30	35	2 00	25	174,250	5,634	
2– 8	1,536,600	1,716,560	40		1 00	15	179,960		
2–10	1,822,400	2,040,000	40	40	1 45	15	217,600		
2–12	1,715,200	1,798,400	40	45	1 50	15	83,200		
2–15	1,904,000	1,910,400	40		2 00	20	6,400		
2–17	1,800,000	1,940,800	45		2 10	30	140,000		
		1,888,000			2 35				
2–21	2,009,600	2,118,400	50	55	2 00	15	108,000		
2–23	2,187,200	2,176,000	50	50	2 15	10			
2–24	1,932,800	2,100,800	50	55	1 45	15	168,000		
2–27	2,137,600	2,172,800	50	55	1 00	30	35,200		
		2,540,800		60	1 40		403,200		
3– 1	2,257,600	2,288,000	55	55	1 00	25	30,400		
		2,448,000		60	1 45		190,400		
3– 4	2,129,600	2,232,800	50	55	1 30	20	103,200		
3–13	2,498,400	2,590,400	50		2 00	20	92,000		
3–20	2,441,600	2,550,400		65	1 30	25	108,800		

* B,—before massage. A,—after massage.
Note observation on Feb. 27. Little increase at 1 hour, marked increase at 1 hr. 40 minutes.

Roth isolated the spleen and confirmed the work done by others, which had determined that quinine given subcutaneously to dogs brings about contraction of the spleen. He then studied the effect of splenic contraction on the blood cells and came to the conclusion that the changes induced by the quinine "may be due to mechanical forces entirely, namely, the contraction of the organs which harbor large numbers of lymphocytes."

Lamson (10) and Kieth have shown that epinephrin causes an increase in the red cells per volume of blood in animals. They seem to have shown conclusively that this increase is due to the action of the epinephrin on the liver, for when they excluded the liver from the general circulation the injection of epinephrin had no such effect on the red cells. On the other hand, under these conditions the epi-

nephrin caused a decrease in the plasma volume similar to that induced by sweating and diarrhea, but without the proportional increase in cells that accompanies these conditions. This observation lends support to the idea that a proportional number of corpuscles was destroyed or driven from the general circulation. Lamson and Kieth explain this phenomenon on the grounds that epinephrin under all conditions causes a decrease in the plasma volume and when the liver is not shut off, the normal flow of red cells into the circulation continues, and apparently in addition to this the discharge of corpuscles from the liver is increased, as the reduction of plasma does not account entirely for the increased count.

One might argue that because of the increase in the red cells the increase in the white cells is relative or proportional. In Cases XVI and XVII I have plotted a curve on the graphic chart which shows the ratio between the red and white corpuscles. The base line represents the ratio in the control counts. In Case XVII the average ratio in the control counts is 1 white to 664 red cells. If there is an actual increase in the number of white cells in the blood, the ratio at the time of the increase in the reds should be low. We find at 9:30, when the red cells reach their highest point, the ratio *is low*, 1–475. Putting it another way, at this time if the control ratio is maintained there should be 10,129 white cells; there are 13,850, 3721 more than there should be on this hypothesis. At 10:00, when the red cells reach their lowest range, there should be 6204 white cells. This is practically the number we find. In both experiments the tendency is to a low ratio at the time when the red count is high.

There is one more point that must be considered—the prolonged effect of the adrenalin. We have observed this effect not only on the formed elements of the blood, but also on blood sugar curves induced by adrenalin (1). It is probable that a hormone action is responsible for this finding.

In Case XVII at 9:15 there is a beginning increase in the red cells. At this time the patient was shaking hard, her hands were cold, stiff, and clammy. The blood flowed very slowly from the finger. At 9:30, when the red cells reached their highest point, these symptoms were less marked, and the blood flowed freely from the finger.

From these observations, it appears that the increase in the

white cells following adrenalin is not entirely proportional, and must be due, in part, to the discharge into the circulation of extra numbers of leucocytes from the cell depots. As Lamson's experiments show that, in addition to the increase in red cells that would come from a decrease in the plasma volume by the adrenalin, there is an overdischarge of red cells from the liver, so Roth's experiments show that there is an overdischarge of lymphocytes from the spleen due to splenic contraction.

Since we know that adrenalin similarly contracts the spleen, that the white cell changes after adrenalin are practically the same as those produced by quinine, and that the red cell changes are the same as those induced by massage, one feels justified in concluding that the changes in the blood cells induced by adrenalin are purely mechanical, and are not due to an increased histogenesis, as we believe is the case with the blood changes following intravenous injection of typhoid protein.

Conclusions. 1. The intramuscular injection of 1 mg. of adrenalin causes an increase in the leucocytes. There is an initial rise, followed by a decline, which usually takes place within one-half to one hour, a secondary increase in the leucocytes begins at the second hour and may continue above the control counts until the eighth hour. A distinct leucocytosis is often induced.

2. There is a distinct tendency for the lymphocytes to rise very soon after the injection. This increase is not long sustained. The rise is usually relative, but may be absolute, and it is usually coincident with a rise in the polymorphonuclears. A secondary rise occurs, but not so constantly as is that of the polymorphonuclears.

3. The acidophile lymphocyte is increased in numbers after the injection of adrenalin. The greatest increase usually comes one-half hour after the injection.

4. Adrenalin causes an abrupt and marked rise in the erythrocytes during the first half hour. At the end of this time they may have returned to normal. A secondary rise occurs at 1½ to two hours after the injection, and may be sustained for three hours.

5. The increase in the red cells is similar to the increase induced by general massage.

6. The changes in the blood cells induced by intramuscular injection of adrenalin are purely mechanical and are not due to an

increased histogenesis, as we believe is the case with intravenous injection of typhoid protein.

BIBLIOGRAPHY

1. Cowie and Beaven, "On the Clinical Evidence of Involvement of the Adrenal Glands in Influenza and Influenza Pneumonia." In press.
2. Hatigan, J., *Wien. klin. Wchnschr.*, 1917, XXX, 1541. Ab. *Endocrinology*, 1918, p. 161.
3. Cowie and Beaven, "Nonspecific Protein Therapy (Typhoid Protein) in Influenza Pneumonia," *J. Am. M. Ass.*, April 19, 1919, 1117.
4. Cowie and Calhoun, "Nonspecific Protein Therapy in Arthritis and Infections," *Arch. Int. Med.*, Jan. 1919, XXIII, 69–131.
5. Castren, H., "Finska Läkaresällskapets Handlinger" (Helsingfors) 1916, LVIII, 1605. Ab. *Endocrinology*, I, 400.
6. Oliver, *Lancet*, 1896, I, 1778. Quoted by Ewing, "Clin. Pathol. of the Blood," Sec. Ed., 1903.
7. Mitchell, John K., "The Effect of Massage on the Number and Hemoglobin Content of the Red Blood Cells," *Am. J. Med Sc.*, 1894, CVII, 502.
8. Ekgren, *Deutsche med. Wchnschr.*, 1902, 519. Quoted by Ewing, loc. cit.
9. Roth, Geo. B., "The Action of Quinine on the Leucocytes," *J. Pharmacol. & Exper. Therap.*, 1912–13, IV, 157–165.
10. Lamson, P. D., Jr., *Pharmacol. & Exper. Therap.*, 1916, VIII, 167 and 130, Lamson and Kieth, *ibid.*, 247–251.

STUDIES ON BLOOD SUGAR

EFFECTS UPON THE BLOOD SUGAR OF THE REPEATED INDIGESTION OF GLUCOSE

By Louis Hamman

In a communication to the *Archives of Internal Medicine* Hamman and Hirschmann(1) have demonstrated the blood-sugar response to the ingestion of a single large dose of glucose in normal persons and in others suffering from various diseases. For this study 100 grams of glucose were administered in the early morning after the night fast, and the blood sugar and urine sugar estimated at short intervals thereafter. It was demonstrated that there are two important types of reaction, the normal and the diabetic. There is still a third type, not nearly so clearly distinguished as these two, the reaction of increased carbohydrate tolerance. Although the reaction in normal persons varies in different individuals and in the same individual under different circumstances, its general characters are as follows: The blood sugar rises rapidly, but seldom exceeds 0.15 per cent; it falls somewhat more slowly to the original level, the whole reaction being over in less than two hours. In diabetics the rise is higher and longer sustained. If the blood sugar surpasses 0.18 per cent, sugar usually appears in the urine, but sometimes it appears at a somewhat lower level; at other times it fails to appear, even though 0.2 per cent of blood sugar is exceeded. From two to five hours pass before the blood sugar reaches the original fasting level. When the carbohydrate tolerance is increased, there is only an insignificant rise in the blood sugar, which has usually a low fasting level.

Epstein (2) and Woodyat (3) have raised the objection that these variations in blood sugar following the ingestion of glucose represent, not real variations in the sugar content of the blood, but apparent variations due to changing blood volume. This possibility

had suggested itself to us, but the investigations of Mosenthal and Hiller (4) show conclusively that there is no constant relation between variations in blood sugar percentage and the water content of the blood. Indeed, these two factors show such bizarre relations that the one surely cannot depend entirely upon the other.

There is every possible gradation in the response to glucose ingestion, from the low, insignificant curve of high glucose tolerance to the extreme and prolonged curve obtained in severe diabetes. However, the so-called diabetic curve is not peculiar to diabetes, for similar curves, though usually not so extreme, are obtained with nephritis, in hyperthyroidism, and in many other conditions of lowered carbohydrate tolerance. These innumerable gradations force upon us the conviction that disturbances of carbohydrate tolerance are quantitative, not qualitative, variations. In other words, that diabetes represents functionally a disturbed, not an altered, mechanism of carbohydrate control.

For many years investigators have sought to distinguish between the glycosuria of diabetes and the glycosuria due to a great variety of other conditions. Of the many distinguishing marks that have been proposed only two (5) are still urged as pertinent, namely, the parodoxical law of Allen and the diuretic effect of sugar in diabetes. When sugar is injected intravenously in large quantity it acts as a diuretic; administered otherwise, it diminishes the output of urine. In diabetes sugar acts as a diuretic by whatever route it be administered. While this distinction is true between normal and totally diabetic animals, it is only relatively true in human beings.

The ease with which sugar acts as a diuretic depends upon the degree of diabetes; in mild cases conditions are much nearer the normal than the completely diabetic. In other words, the ease with which sugar produces diuresis depends directly upon the degree of carbohydrate tolerance, and it varies with this tolerance. Here again the distinction is purely quantitative, and the varying diuretic effect of sugar surely cannot be pointed out as a mark of distinction between diabetes and other glycosurias. How convincingly the observations of Woodyat and his co-workers (6) confirm this statement! By carefully measured and timed intravenous injections of

glucose the tolerance of an individual can be accurately determined, and sugar begins to act as a diuretic when this limit is overstepped.

Therefore the only remaining feature that can be drawn upon to point a qualitative distinction between diabetes and other glycosurias is Allen's parodoxical law. Allen (7) enunciates this law in these words: "Whereas in normal individuals the more sugar is given the more is utilized, the reverse is true in diabetes." Apparently this law was enunciated to fit conditions in totally diabetic animals, where it applies aptly enough, but if we properly understand what is meant by the law, it is not applicable to diabetes in human beings.

When carbohydrate tolerance is only mildly reduced, the level of tolerance is by no means absolute. For instance, if the ingestion of 50 grams of glucose be followed by the excretion of 1 gram of glucose in the urine, it does not follow the ingestion of 100 grams will cause an excretion of 51 grams. Far from it. Such experiments have been frequently made, and but a small proportion of the excess is recovered from the urine. Only when excessive amounts of glucose are administered intravenously and at a uniform rate is the proportion of excretion constant. Here, again, the difference seems distinctly to be quantitative and not qualitative. It occurred to me that further important evidence bearing upon this point could be obtained by testing the reaction of patients to the repeated ingestion of glucose. If there be a qualitative difference in the utilization of glucose by normal persons and by diabetics, then such tests should certainly give evidence of the difference. The only observations upon this point that I was able to find in the literature are a few experiments upon rabbits reported by Bang. In normal rabbits Bang (8) finds that the second administration of a certain dose of glucose given during the decline of the reaction from the first administration is followed by a much less marked reaction than was the first.

Experimental Results. In normal persons the administration of a second dose of glucose immediately after the reaction to the first dose produces a much less marked reaction upon the blood sugar than did the first dose. The protocols of two experiments illustrate this.

Experiment I. E. L. C., male, single. Age twenty-eight. Healthy physician.

Time	Blood Sugar, Per Cent	Urine c.c. per Hour	Urine Sugar, Gm. per Hour
8.30	0·086 Glucose: 100 gm.	in 300 c.c. water.	
9.00	0·118	88	0
9.30	0·110	74	0
10.30	0·087 Glucose: 100 gm.	162 in 300 c.c. water.	0
11.00	0·087	150	0
11.30	0·078	150	0
12.30	0·096 Glucose: 100 gm.	111 in 300 c.c. water.	0
1.00	0·080	31	0
1.30	0·087	26	0
2.30	0·094	26	0

Experiment II. B. H., male, single. Age twenty-nine. Healthy physician. Patient previously tested had shown a low renal threshold; that is, sugar had appeared in the urine when the blood sugar reached 0.14 per cent.

Time	Blood Sugar, Per Cent	Urine c.c. per Hour	Urine Sugar, Gm. per Hour
9.15	0.110	28	0
9.16	Glucose: 100 gm.	in 300 c.c. water.	
9.45	0·162	28	trace
10.15	0·127	30	trace
10.45	0·130	26	0
10.50	Glucose: 100 gm.	in 300 c.c. water.	
11.20	0·110	28	0
11.50	0·122	21	0
12.20	0·115	26	0

These experiments indicate that the mechanism of carbohydrate utilization, once stimulated, works more efficiently than when called upon abruptly to manage large amounts of glucose. Probably to this fact is largely due the better utilization of sugar slowly absorbed, and the almost unlimited power of the body to utilize starch.

In diabetics the same difference is observed as in normal persons; the following protocols illustrate this, although the difference is not so marked.

Experiment III. A. B., male, white, married. Age forty-six. Dispensary No. 46,750. A moderately severe diabetic who had become sugar-free on a carbohydrate-free diet.

Time	Blood Sugar, Per Cent	Urine c.c. per Hour	Urine Sugar, Gm. per Hour
8.25	0·161	42	0
8.30	Glucose: 20 gm.	in 300 c.c. water.	
9.00	0·205	51	0·3
9.32	0·244	56	1·57
10.30	0·196	45	0·9
11.30	0·180	68	0·66
11.35	Glucose: 20 gm.	in 300 c.c. water.	
12.05	0·161	63	0·23
12.30	0·188	55	0·26
1.30	0·205	117	0·44
2.30	0·164	113	0·34

Experiment IV. A. T., male, white, married. Age forty. Hospital No. 37,026. Diagnosis: Hypertension, myocardial insufficiency, emphysema, arteriosclerosis, diabetes mellitus, obesity. Patient had only small amount of sugar in urine, easily controlled by moderate regulation of diet.

Time	Blood Sugar, Per Cent	Urine c.c. per Hour	Urine Sugar, Gm. per Hour
8.35	0·150	4	0
8.38	Glucose: 100 gm.	in 300 c.c. water.	
9.10	0·206	5	0
9.42	0·272	33	0·68
10.45	0·222	76	2·66
11.15	0·190	49	1·63
11.18	Glucose: 100 gm.	in 300 c.c. water.	
11.45	0·212	41	1·36
12.27	0·209	54	1·69
12.57	0·173	37	0·56

Persons with lowered carbohydrate tolerance, but not outspoken diabetes, react in a similar way. Even if the second dose of glucose be much larger than the first, the reaction following is not so marked.

Experiment V. W. G., male, white, single. Age forty-seven. Hospital No. 36,926. The patient had a mild infection of unknown cause and mental symptoms. No definite medical diagnosis made. Sugar never found in urine on ordinary ward diet.

Time	Blood Sugar, Per Cent	Urine c.c. per Hour	Urine Sugar, Gm. per Hour
8.40	0.120	8.5	0
8.49	Glucose: 50 gm. in	300 c.c. water.	
9.20	0.176	314	0
9.53	0.200	463	1.7
10.55	0.166	242	0.8
10.57	Glucose: 50 gm. in	300 c.c. water.	
11.30	0.178	246	0.5
12.00	0.136	132	0.6
12.45	0.130	79	0

Experiment VI. J. H., male, black, married. Age thirty-nine. Surgical No. 42,151. Diagnosis: Exophthalmic goiter, adenoma of thyroid. No sugar found in urine on usual ward diet.

Time	Blood Sugar, Per Cent	Urine c.c. per Hour	Urine Sugar, Gm. per Hour
8.30	0.097	36	0
	Glucose: 100 gm. in	300 c.c. water.	
9.00	0.130	64	0
9.30	0.196	31	0
10.05	0.177	73	0
10.45	0.161	49	0
11.00	Glucose: 100 gm. in	300 c.c. water.	
11.30	0.173	57	0
12.00	0.164	142	0
12.30	0.148		
1.00	0.116	25	0

Experiment VII. A. N., male, white, married. Age thirty-seven. Medical No. 36,828. Diagnosis: Bilateral facial palsy, psychoneurosis. No sugar appeared in urine on ordinary ward diet.

Time	Blood Sugar, Per Cent	Urine c.c. per Hour	Urine Sugar, Gm. per Hour
8.25	0.093		
8.30	Glucose: 100 gm. in	300 c.c. water.	
9.00	0.161	32	0
9.30	0.096	97	0
10.05	0.100	129	0
10.07	Glucose: 150 gm. in	300 c.c. water.	
10.35	0.148	84	0
11.05	0.097	60	0
11.36	0.094	114	0

In the following patient the utilization of glucose is normal,

although a small amount of sugar appears in the urine. The patient has a low renal threshold, that is a mild grade of renal diabetes.

Experiment VIII. W. A. C., male, white, married. Age thirty-six. Diagnosis: Hyperthyroidism, psychoneurosis, renal diabetes. Small amount of sugar occasionally found in urine. Considerable sugar in urine after ingestion of 75 gm. of glucose.

Time	Blood Sugar, Per Cent	Urine c.c. per Hour	Urine Sugar, Gm. per Hour
8.30	0.088	43	0
8.40	Glucose: 100 gm. in	300 c.c. water.	
9.10	0.125	92	trace
9.35	Glucose: 100 gm. in	300 c.c. water.	
9.43	0.105	251	0.2
10.10	0.085	658	0
10.50	0.084	216	0
11.40	0.084	68	0

It was found in testing several patients that they reacted to levulose in the same way that they did to glucose, only the blood sugar rise was less marked. For instance, the diabetic whose response to glucose is detailed in Experiment III gave the following response to levulose:

Experiment IX. A. B. Same patient as in Experiment No. III. Male, white, married. Age forty-six. Dispensary No. 46,750. A moderately severe diabetic who had become sugar-free on a carbohydrate-free diet.

Time	Blood Sugar, Per Cent	Urine c.c. per Hour	Urine Sugar, Gm. per Hour
8.30	0.167	66	0
8.34	Levulose: 20 gm. in	300 c.c. water.	
9.01	0.177	36	0
9.33	0.194	68	0.5
10.32	0.177	150	0
11.00	0.177	329	0
11.02	Levulose: 20 gm. in	300 c.c. water.	
11.35	0.167	178	0
12.10	0.184	103	0
1.00	0.184	144	0

Conclusions. 1. The ingestion of glucose in some way stimulates the mechanism of carbohydrate disposal so that the repeated ingestion of the same amount causes a less marked hyperglycemia.

2. The same stimulating effect is noted in diabetes; the second

dose is followed by a less marked hyperglycemia and glycosuria. However, the difference between the effects of the two doses is less marked than in normals, and varies in different stages of the disease. Perhaps when the diabetes is very severe the difference may completely vanish.

3. In renal glycosuria the normal stimulating effect of the ingestion of glucose is retained.

4. Levulose produces a much less marked hyperglycemia and glycosuria than does an equal amount of glucose.

5. The difference in the reaction of the normal and the diabetic is a quantitative, not a qualitative, difference.

BIBLIOGRAPHY

1. Hamman and Hirschman, *Arch. Int. Med.*, 1917, XX, 761.
2. Epstein, Discussion, *Soc. for Clinical Inves.*, May, 1916.
3. Woodyat, Discussion, *Ass. Am. Phys.*, May, 1917.
4. Mosenthal and Hiller, *J. Biol. Chem.*, 1916, XXVIII, 197.
5. Joslin, "Treatment of Diabetes Mellitus," 2d Edition, 1917.
6. Woodyat, Sansum, and Wilder, *J. Am. M. Ass.*, 1915, LXV, 2067.
7. Allen, "Glycosuria and Diabetes," 1913, Harvard Univ. Press.
8. Bang, "Der Blutzucker," Wiesbaden, 1913.

INFLUENCE OF FAT ON CALCIUM METABOLISM

By B. Raymond Hoobler, M.D., Detroit, Mich.
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THERE have been many researches conducted in recent years which have demonstrated that calcium metabolism is closely connected with the functioning of the nervous system, as well as being of prime importance in the up-building of the bony structures of the body.

A negative calcium balance cannot long exist without producing profound changes in the life processes of the individual. When such a condition exists it would seem a very easy thing to change a negative to a positive balance by the simple procedure of administering calcium in the form of the lactate or chloride, but such administration is not always accompanied by an increase in the retention of calcium. During a series of observations on infants and young children it was found that the absorption and retention of calcium was markedly affected by the amount and kind of fat in the diet of the individual to whom the calcium was administered.

A group of children were put on a measured diet, and their calcium absorption and retention were obtained. They were then continued on the same diet, but additional fat was administered in the form of cod liver oil. Each child showed that the aggregate of calcium, both absorbed and retained, declined to the extent of 50 per cent in some instances. A chart is submitted showing these results.

This observation has a very important bearing on the treatment of rachitis and tetany, many clinicians preferring to use cod liver oil and phosphorus. It would seem that this procedure would lessen calcium retention and add to the difficulty rather than correct it. A further interesting observation was made regarding the effect on calcium retention of a diet containing quantities of milk fat. The results of such observations indicate that the per cent both of calcium absorbed and retained is increased as the milk fat in the diet is increased, Chart II, showing absorption, Chart III retention

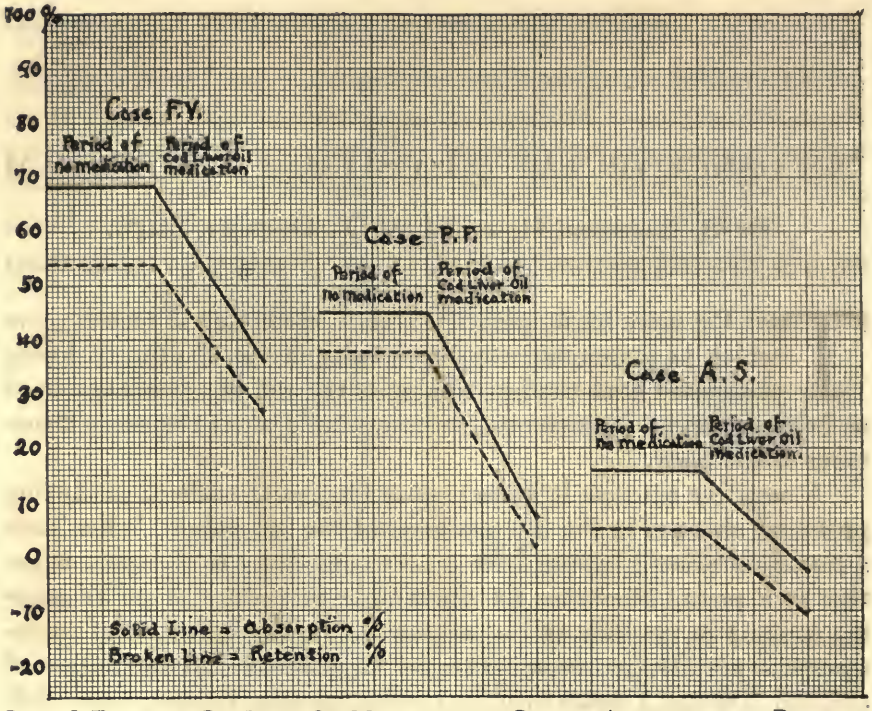

CHART I. EFFECT OF COD LIVER OIL MEDICATION ON CALCIUM ABSORPTION AND RETENTION

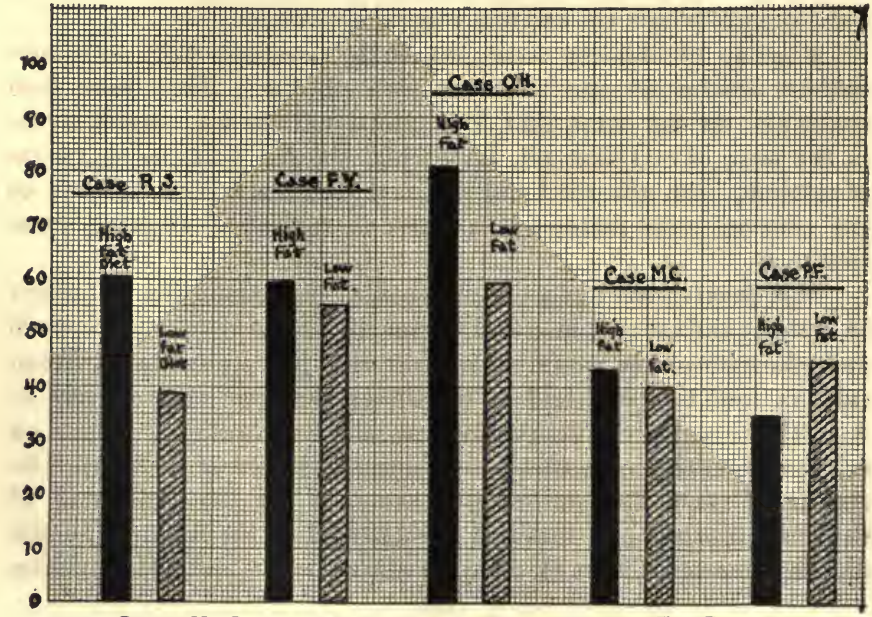

CHART II. CALCIUM ABSORPTION ON HIGH AND LOW FAT DIETS

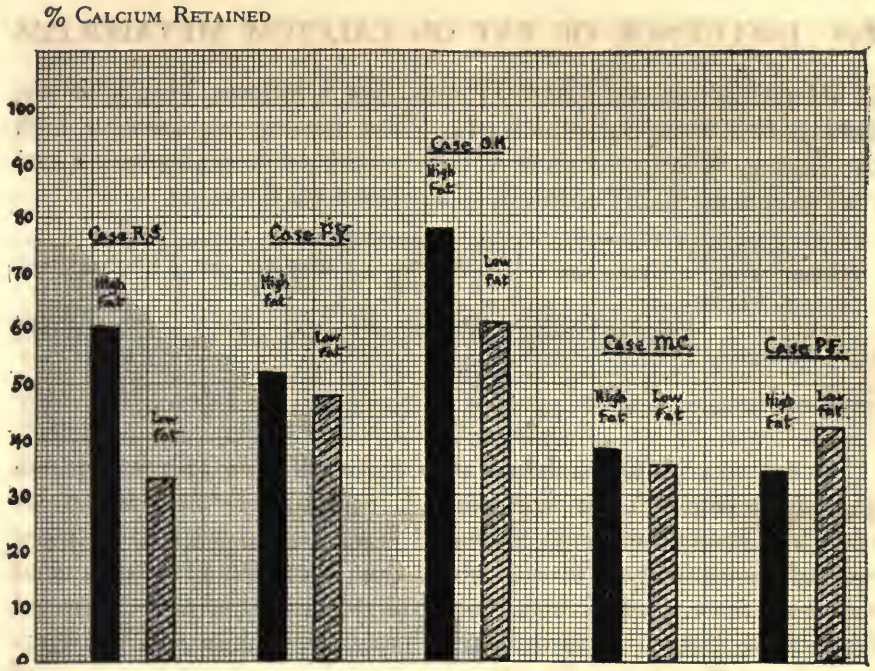

Chart III. Calcium Retention on High and Low Fat Diets

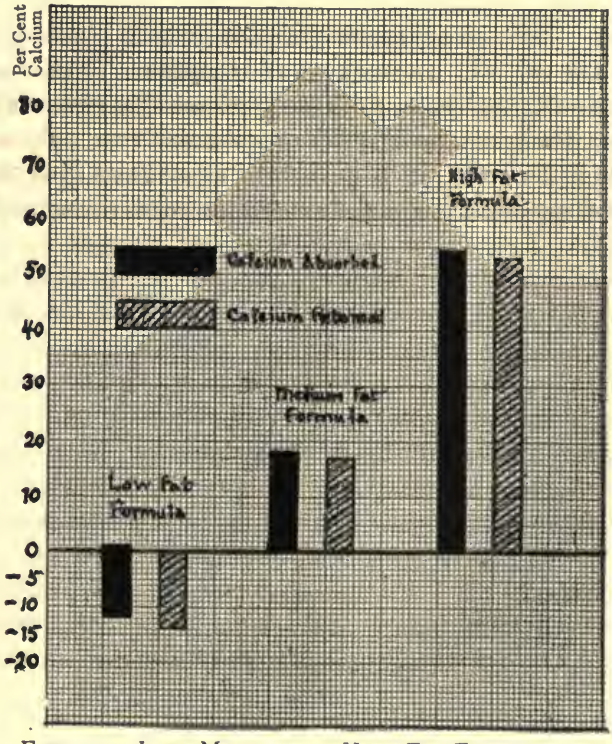

Chart IV. Effect of Low, Medium and High Fat Formulas on the Calcium Metabolism of Healthy Infant

in older children, and Chart IV retention in infants. This, however, holds only in those individuals who do not develop an acidosis on high fat feeding. When acidosis does develop the calcium absorption and retention is markedly reduced, as is whown by the table.

Period	Fat in Food, Grams	Calcium		Ammonia in Urine		Acetone and Diacetic		β-oxybutyric Acid	
		Per Cent Absorbed	Per Cent Retained	Abs. Amt.	Per Cent T. Nit.	Abs. Amt.	Per Cent of Urine	Abs. Amt.	Per Cent of Urine
First	70.04	79.9	79.5	0.2694	5.4	.0	.0	.2905	.392
Second	70.04	79.9	79.7	0.8232	18.6	.278	.066	.8625	.205
Third	70.04	4.0	3.6	1.5534	30.4	.593	.078	1.767	.232

It will be seen that calcium absorption fell from 79.9 per cent to 4 per cent, and calcium retention fell from 79.5 per cent to 3.6 per cent, as urinary ammonia increased from 5.4 per cent to 30.4 per cent of total nitrogen, during which time acetone and diacetic acid increased from none to .593 gram, and β-oxybutyric acid increased from .2905 gram to 1.767 grams in twenty-four hours. The observation was discontinued in the next period because of the onset of vomiting.

Summary. These observations indicate (*a*) that cod liver oil tends to diminish the calcium absorption and retention; (*b*) that increasing quantities of milk fat tends to favor calcium absorption and retention; (*c*) that the last-named observation holds true only as long as the individual does not develop a state of acidosis, but that when acidosis develops calcium absorption and retention practically cease.

ON CONTRA-LATERAL REPRESENTATION IN THE CEREBRAL CORTEX OF THE PERIPHERAL BLOOD VESSELS

By S. P. Kramer, Cincinnati, O.

In May, 1909,[1] while removing a large cortical tumor from the left rolandic area, it was noticed that the radial pulse on the contra-lateral or right side became markedly "weaker" than that on the left. This occurred at both the preliminary and final operations, and the difference in the two pulses was evident for some hours after the operative procedures. Since then I have had an opportunity to record a similar phenomenon in two traumatic cases involving the cerebral cortex in which there was a measured difference in blood pressure (Riva Rocci) of 15 and 20 mm. of mercury. That is, the blood pressure in the radial artery of the extremity opposite the side of the cortical lesion was so much lower than the pressure on the other side.

The clinical experiences above referred to called for an investigation into the possible changes in pressure in the vessels of the extremities as the result of stimulation of their contra-lateral cortical centers. For this purpose the line of experiment consisted in registering the changes in pressure in the distal end of the divided femoral artery. The artery was divided well below the profunda branch. The peripheral pressure recorded there varied in different animals between 30 and 80 mm. This amount of pressure probably depends on the collateral circulation, but it was *a priori* reasonable that any change in the caliber of all the vessels of the extremity below the point of ligature would manifest itself plainly by influencing the pressure as measured in the distal end of the divided artery. Accordingly the leg area of the cortex cerebri on both sides was stimulated alternately and the pressure in the peripheral ends of both femoral arteries was recorded. The animals were anesthetized with ether, after which tracheotomy was performed

[1] *N. York M. J.*, Zenner and Kramer, October 2, 1909.

and ether administered through the tracheal tube. The changes in the central and peripheral blood pressure were recorded by mercury manometers connected with canulæ in the central end of carotid artery for the central or general blood pressure, and the distal ends of the divided femoral arteries for the peripheral pressure. The femoral canulæ were always placed distal to the giving off of the profunda branch. In some experiments changes in the volume of the posterior extremity were recorded by means of a plethsphygmograph connected with a water monometer. The cerebral cortex was stimulated electrically (faradic) by means of a Kronecker coil connected with platinum electrodes (bi-polar). An electric signal placed in the primary circuit registered the period of stimulation.

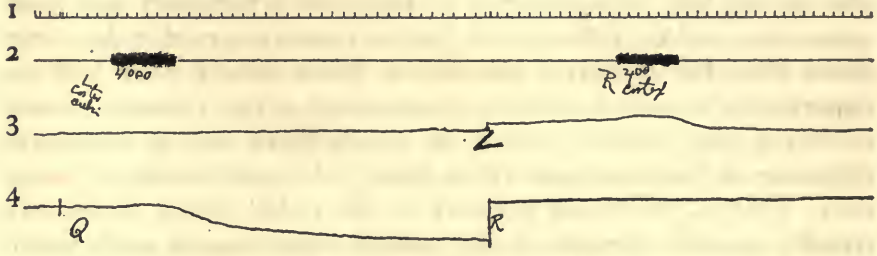

FIG. 1. DOG, JULY 10, 1910.

1. Seconds. 2. Period and Amount of Stimulation. 3. Left Peripheral Pressure (Femoral). 4. Right Peripheral Pressure (Femoral).

On stimulating the motor area of the cortex of a dog with currents of moderate intensity and with light anesthesia the general blood pressure as measured in the carotid artery showed a marked fall. This fall comes on a few seconds after the beginning of the irritation, lasts a varying period after the cessation of the stimulation, to return again usually inside of half a minute to the pressure that obtained before the irritation. This fall in pressure may be preceded by a momentary rise, very slight in extent and not lasting over two seconds. If, now, the anesthesia be deepened by administering more ether, this effect with the same amount of stimulation does not occur. Further, if the electrodes be applied to an indifferent part of the cortex, i.e., outside the motor area, this effect, i.e., this drop in blood pressure, does not manifest itself.

Fig. 1 is a tracing in which the record is given of an experiment in which the left and right leg areas of the cerebral cortex were

alternately stimulated by the application of 4000 Kronecker units, while the peripheral pressure in both femoral arteries was recorded. It will be seen by referring to Fig. 1 that, when the left leg area in the cortex was stimulated, the peripheral blood pressure in the right femoral artery fell; and that when immediately thereafter the same stimulus was applied to the right leg area, the peripheral pressure in the left femoral artery fell.

In a second tracing, Fig. 2, the circulatory conditions of the whole investigation are epitomized. Here three manometers were

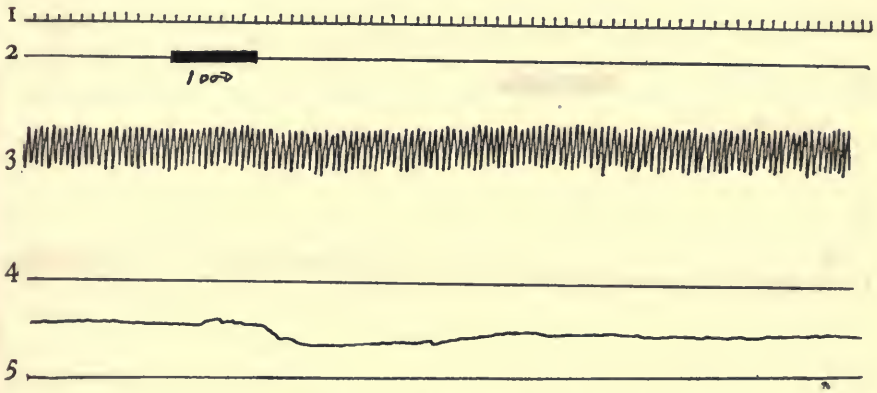

FIG. 2. DOG, AUGUST 3, 1910.

1. Seconds. 2. Period and Amount of Stimulation of Left Leg Area of Cortex Cerebri. 3. Central Blood Pressure (Left Carotid). 4. Peripheral Blood Pressure (Left Femoral Artery). 5. Peripheral Blood Pressure (Right Femoral Artery).

applied; one inserted in the central end of the carotid artery registered the general blood pressure. The other two were connected with the distal ends of the divided femoral arteries. A stimulus of 4000 units was applied to the left cortical leg area. There followed a marked fall in the general blood pressure (preceded by a slight momentary rise); practically no change in the peripheral pressure in the left femoral artery, and a marked drop in the peripheral pressure in the right femoral. Now, either by gradually increasing the anesthesia, or by diminishing the amount of stimulus, one can arrive at a degree of stimulation which will cause the drop in peripheral pressure on the contra-lateral side and leave the general pressure and the peripheral pressure on the homolateral side unchanged. This is shown by the tracing in Fig. 2.

These results are independent of the influence of muscle contractions, and of the action of the vagi nerves, for they are obtained in animals that are curarized and after section of the vagi. The preliminary rise spoken of, which sometimes precedes the fall in pressure, disappears when curare is given; an indication that this, however, is due to the direct mechanical pressure of the contracting muscles on the blood vessels.

That the fall in peripheral pressure is due to a true dilatation of the vessels of the extremity is supported by the fact that it can be

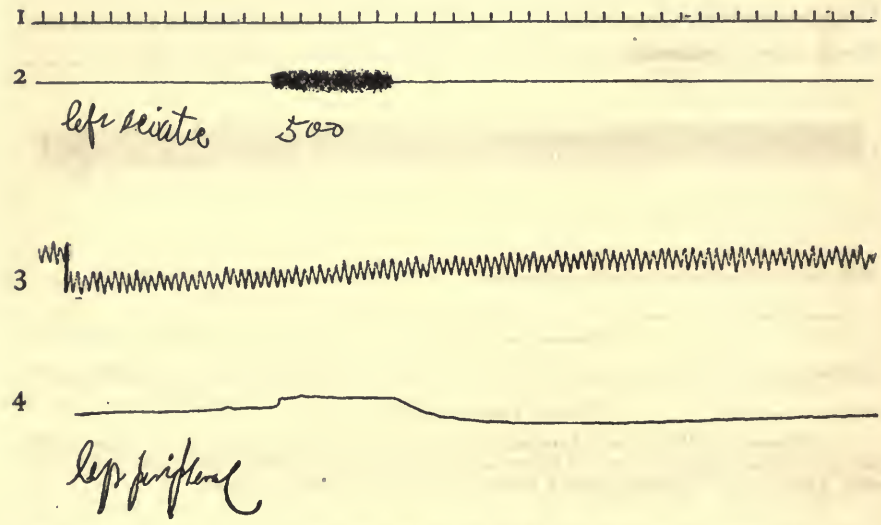

FIG. 3. DOG, JULY 18, 1910.

1. Seconds. 2. Period and Amount of Stimulation. 3. Central Blood Pressure (Left Carotid Artery). 4. Peripheral Blood Pressure (Left Temporal Artery).

produced by weak stimulation of the peripheral end of the divided sciatic nerve. (Shown in Fig. 3.) The injection of adrenalin into the femoral artery of course causes a rise in the peripheral pressure.

The experiments described above were done in the laboratory of my lamented friend and master, Sir Victor Horsley, during the summer of 1910. They have heretofore not been published, and the original manuscript with corrections in his handwriting is one of my most cherished mementoes.

COLLOID CHEMISTRY AND MEDICINE

By Jacques Loeb, M.D., New York

(From the Laboratories of The Rockefeller Institute for Medical Research)

THE development of medicine and biology will be influenced to a considerable extent by our conception of the nature of the reactions between crystalloids and colloids, since a large part of the reacting material of the body is colloidal. The only definition of colloids which does not go beyond the facts is, as far as the writer is aware, that colloids cannot diffuse through parchment (or similar) membranes, which are permeable for crystalloids. It is assumed by many that the laws of classical chemistry do not apply to the behavior of colloids; and those who hold such views call themselves "colloid chemists." This school by no means includes all the workers on colloids or proteins; on the contrary, authorities on bio-colloids, like Hardy, Sörensen, Robertson, and others, take the opposite view. Since, however, colloid chemists have found medicine a promising field for propaganda, it may seem pardonable to pass in review some of their methods and claims.

The writer is under the impression that this new development of "colloid chemistry" was largely influenced by a temporary error into which Wilhelm Ostwald had fallen, namely, that atoms and molecules had no real existence. During Ostwald's period of warfare against "scientific materialism" some of his followers seized upon the colloids as the means of creating a chemistry free from the conception of the real existence of atoms and molecules. Thus Freundlich tried to show that the interaction between colloids and crystalloids did not follow the law of mass action, but a different law, his so-called adsorption formula; and reactions between colloids and crystalloids were not supposed to occur in stoichiometrical relations; it was also claimed that solutions of colloids were not real solutions, and that the osmotic phenomena observed in such solutions could not be explained on the basis of classical physical

chemistry. Notwithstanding the fact that the complete proof of the real existence of atoms and molecules has abolished the justification of the dream of a non-chemical "colloid chemistry," the movement has continued to spread.

When Ehrlich appealed to Arrhenius to prove, if possible, that the phenomena of immunochemistry were chemical in character, Arrhenius approached the problem in the only way possible, namely, from the viewpoint of the law of mass action. He could show that certain reactions in immunochemistry occurred similarly as in the interaction between a weak base and a weak acid. (1) Unfortunately his investigation brought to light more than was compatible with Ehrlich's side-chain theory. In this situation Ehrlich and his followers disavowed classical chemistry and accepted the escape offered by "colloid chemistry." As a consequence the phenomena in immunochemistry are to-day frequently discussed in terms of adsorption. As long as these discussions are based upon merely qualitative experiments or consist merely in assertions that the phenomena in question are "colloidal" or "adsorptive" and not chemical, they may be passed over as verbalisms. They become worthy of consideration when they are quantitative in character, purporting to prove that the phenomena in question obey the adsorption formula of Freundlich in contradistinction to the law of chemical mass action. In this connection it is of great significance that one of the leading physical chemists in this country, Mr. Irving Langmuir, (2) has recently investigated the adsorption of gases on plane surfaces of glass, mica, and platinum, where the purely chemical character of the forces was much more obscure and difficult to prove than in the case of the reaction between electrolytes and proteins. He was able to show that "the forces causing adsorption are typically chemical," and that only the same primary and secondary valence forces are active which act in any of the ordinary typical chemical reactions. Stoichiometric relations only fail to hold where "steric hindrance effects" or experimental obstacles and shortcomings interfere. As far as Freundlich's adsorption equation is concerned, Langmuir states "that it agrees very poorly with experiments when the range of pressure is large." Langmuir's investigations leave little doubt that the adsorption formula is only the result of accidental experimental difficulties. Where these

difficulties are overcome or taken into due consideration the laws of classical chemistry seem to hold.

II. A second field in medicine where colloid chemistry has made itself felt lies in the discussion of the exchange of water between cells and the surrounding liquid—blood or lymph in animals or the sap in plants. Whatever special conception of the mechanism of osmosis may be held, the kinetic theory demands that the osmotic pressure be determined by the number of particles—molecules or ions—in solution (or suspension). Thus whenever tissues or cells are surrounded by membranes which are permeable to water but impermeable to either salts or proteins dissolved or suspended in the cell sap, a diffusion of water must occur until osmotic equilibrium is established, i.e., until in the unit of time as many molecules of water (and of other substances capable of diffusing through the membrane) diffuse into the cell or tissue as diffuse out. The greater the number of non-diffusible molecules or particles in the cell the higher the hydrostatic pressure upon the cell contents must become before this statistical equilibrium of diffusion is established. Since the non-belief in the existence of the molecule implied also a non-belief in the kinetic theory of gases and liquids, the adherents of the system of "colloid chemistry" felt obliged to look for an explanation of the exchange of liquids between cells and their surroundings on a basis other than Avogadro's and van't Hoff's law. Thus as late as 1915 Wolfgang Ostwald, one of the champions of a non-chemical colloid chemistry, published the following statement:

"Recently it has become more and more clear that such membranes and the corresponding osmotic processes are much rarer than had been assumed and that they occur only in limited cases, e.g., plant cells or animal eggs, but that they cannot solve the whole problem. It has become manifest especially by the investigations of Martin H. Fischer, that the water-binding properties of the colloids and not of the molecular constituents of organized matter play the main rôle in the binding and movement of water. We are dealing chiefly with phenomena of hydration (swelling) and dehydration, such as we can also observe in gelatin plates or other dried material."(3)

The writer is not aware that Fischer has demonstrated any such thing as claimed by Ostwald. Fischer (4) merely asserts, without giving any proof, that the swelling of muscle in distilled water is not

due to a difference of the osmotic pressure of the solution of salts and proteins in the muscle and the surrounding water, but to the following hypothetical conditions, namely, that in the muscle acids are present which tend to cause a swelling of the colloids of the muscle. This swelling he furthermore supposes to be prevented by the presence of salts. When, however, the muscle is put into distilled water, he assumes that the salts diffuse out of the muscle, thereby removing the obstacle to the swelling influence of the acid. This he conceives to be the cause of the swelling of the muscle in distilled water. He has not furnished any of the data necessary to even test his assumption, viz., the determination of the pH in the muscle cells; of the isoelectric points of the proteins in the muscle; of the nature and concentration of the salts in the muscle; of the rapidity at which they diffuse out of the muscle. These data must be on hand before Fischer's claims can be taken into consideration.

Long before 1915 it was known that the exchange of water between muscle and surrounding solution is actually determined by the laws of classical physical chemistry. Through the older experiments of Nasse and the writer (5) it had been shown that in neutral solutions of salts the gastrocnemius of a frog neither loses nor takes up water when the osmotic pressure of the salt solution is equal to that of a one-eighth gram-molecular solution of NaCl, regardless of the nature of the salt; and if the concentration of the salt is slightly higher the muscle loses, when the concentration is slightly lower it takes up water. If van't Hoff's law holds for the exchange of water between the muscle and the surrounding fluid we should be able to calculate exactly the molecular concentration of a sugar solution at which the muscle should neither take up nor lose water, namely, it should be that concentration of sugar which has the same number of particles in the unit of volume as an M/8 NaCl solution. This calculated value is for sugar 0.231 gram-molecular. If, however, the exchange of water is determined in the way suggested by Fischer and endorsed by Ostwald, the muscle must swell in any concentration of sugar, since sugar can have no antagonistic action upon the hypothetical swelling effect of the hypothetical acid in the muscle.[1] It has been demonstrated by Overton, (6) Höber, (7) and a number of

[1] This antagonistic effect of a salt is said to be due to the repression of the electrolytic dissociation of the protein salt, on account of the common anion. Sugar, not being an electrolyte, can have no such repressing effect.

other workers, that the gastrocnemius of a frog neither loses nor takes up water when the concentration of the sugar is what it should be if the law of van't Hoff holds for the adsorption of water by the muscle, namely about 0.231 gram-molecular. Moreover, it can easily be shown that the muscle takes up water when the molecular concentration of the sugar is only slightly lower than 0.231 M and that the muscle loses water when the concentration of the sugar is only slightly higher than 0.231 M.

"[This was confirmed for three sugars,] a mono-saccharide, grape sugar; a disaccharide, cane sugar; and a trisaccharide, raffinose. The following table gives the change in weight of the muscle [in per cent of the original weight of the latter] in these solutions in one hour, [the plus sign indicating a gain, the minus sign a loss in weight on the part of the muscle.]

	0·2 M	0·25 M	0·35 M
	Per Cent	Per Cent	Per Cent
Grape sugar	+2·9	−1·6	−7·7
Cane sugar	+3·8	−1·2	−6·1
Raffinose	+1·7	−3·3	−8·9

"The turning point between loss and gain of weight lies for all three sugars between the same limit of molecular concentration, namely, between 0.2 and 0.25 M; and the most important fact is that the value for all three different sugars lies between the limits calculated on the assumption that the exchange of water between muscle and surrounding solution is determined by the Avogadro-van't Hoff law."(8)

We may therefore feel certain that the laws of classical physical chemistry account for the exchange of water between striated muscle and the surrounding liquid and that the vague speculations of Ostwald and other colloid chemists are untenable.

III. The behavior of gelatin, especially the swelling of gelatin plates, has served as a basis for many attempts at explaining life phenomena. Hofmeister (9) compared the amount of swelling of gelatin plates in solutions of different salts and stated that the salts, according to their effects upon swelling, may be divided into two groups. The one group makes gelatin plates swell more than they do in distilled water; the other makes them swell less. The former group includes NaBr, $NaNO_3$, NH_4Cl, NaCl, KCl, while the "dehydrating" group includes the acetates, citrates, tartrates, and sulphates. From these observations colloid chemists have concluded

that it is chiefly the anion which decides the swelling, Cl, Br, NO_3 having a hydrating, while acetates, sulphates, citrates, and tartrates have a dehydrating effect. Hofmeister used rather high concentrations of the salts, and the effects which he observed were very small, so small, indeed, that the writer when he recently read Hofmeister's paper thought he had by mistake gotten hold of the wrong publication. Ralph S. Lillie (10) later claimed to have confirmed Hofmeister's statement on the relative efficiency of the anions in studying the effects of these salts on the osmotic pressure of gelatin solutions. It is also generally assumed that both oppositely charged ions of a neutral salt affect the swelling, acting, however, in an opposite sense, the anion being in general more efficient than the cation. These statements are no longer tenable, owing to the fact that in all these experiments two serious errors were made: first, the effect of the electrolyte upon the gelatin was always measured in the presence of the electrolyte, and second, the hydrogen ion concentration of the solution, in which the gelatin was, was not measured. In avoiding these errors the writer found that the effects of the anion claimed by Hofmeister and the colloid chemists do not exist, and that under the conditions under which Hofmeister's and Lillie's experiments were made the anion of a neutral salt cannot affect the gelatin. (11)

The writer's experiments have led to the result that the behavior of gelatin (and probably of all proteins) is easily understood if we consider it as an amphoteric electrolyte which obeys the laws of classical chemistry. Amphoteric electrolytes are characterized by the fact that they are capable of attaching an acid as well as an alkali. Whether they do the one or the other depends on the hydrogen ion concentration of the surrounding solution. When this hydrogen ion concentration exceeds a critical value—which is called the isoelectric point of the protein—the latter will attach acid molecules and form a salt, dissociating electrolytically into a complex protein cation (containing the H ion of the acid) and an anion, that of the acid used, e.g., HBr or HCl. Such gelatin hydrobromide or hydrochloride can exchange its anion with the anions of neutral salts, but is not affected by the cations of these salts, contrary to the assumptions current in colloid chemistry.

When the hydrogen ion concentration is lower than that defining

the isoelectric point the protein is capable of combining only with alkalies forming metal proteinates which dissociate electrolytically into a positive metal and a negative gelatin ion. Such metal proteinates can exchange only their metal ions with those of neutral salts, but they are not affected by the anions of neutral salts. Since common gelatin solutions have generally a hydrogen ion concentration lower than that of the isoelectric point of gelatin, such gelatin cannot be affected by the anions of a neutral salt, as is claimed in colloid chemistry.

At the isoelectric point the gelatin is practically neither capable of electrolytic dissociation nor capable of reacting with neutral salts, and hence it is affected by neither anion nor cation of a neutral salt. At the isoelectric point the gelatin exists as pure gelatin, i.e., gelatin free from ionogenic impurities.

These statements on gelatin are based on volumetric analyses. The isoelectric point of gelatin was found by Michaelis (12) with the aid of migration experiments in the electric field to lie at pH = 4.7. The writer's experiments have shown that the more the pH exceeds 4.7 the more of the gelatin exists in the form of metal gelatinate. When pH < 4.7, i.e., when gelatin is on the acid side of its isoelectric point, the lower the pH the more gelatin exists as gelatin chloride (if the acid used was HCl). The limit is reached in both directions when all the gelatin is transformed into metal gelatinate or gelatin chloride respectively.

For a qualitative demonstration of these facts we can treat gelatin with silver salts, copper salts, dyes, etc., which modify the color of the gelatin, while for volumetric analyses we may treat gelatin with salts of Ag, Br, Cl, CNS; the amount of these ions in combination with gelatin can be determined by the methods of Volhard.

Fig. 1 gives a demonstration of the fact that silver gelatinate can only exist on the more alkaline side from the isoelectric point of gelatin (pH = 4.7). One gram of finely powdered commercial Cooper's gelatin is put for one hour at 20° into each of a series of beakers containing 100 c.c. of M/16 silver nitrate solution. Cooper's gelatin is impure, consisting mainly of calcium gelatinate and possessing a pH of about 7.0. In the beakers containing the $AgNO_3$ solution the calcium gelatinate is transformed into silver gelatinate. The gelatin of each beaker is then put into a cylindrical funnel,

the $AgNO_3$ solution is allowed to drain off, and more or most of the excess of free $AgNO_3$ left in the capillary spaces between the granules of gelatin is removed by two or more washings with 25 c.c. H_2O each. Then the gelatin in the different funnels is brought to a different pH by perfusing each funnel three times with 25 c.c. of a solution of HNO_3, the concentration of which was different for each funnel. Then the excess of the acid is washed off by four perfusions with distilled water. Since all the funnels have the same diameter the height of the column of gelatin after all the liquid has drained off serves as a measure of the degree of swelling. The gelatin is then made into a 1 per cent solution and put for 20 hours into collodion bags to measure the osmotic pressure. Each collodion bag is surrounded by 400 c.c. distilled water. This allows the further removal by dialysis of any traces of free silver nitrate that may still have been left. All this is done in the dark room. The next day the height of the column of solution in the manometer is measured, the pH of each gelatin solution ascertained, and the quantity of Ag in 25 c.c. 1 per cent gelatin solution is determined by Volhard's method. Twenty c.c. of each gelatin solution are put into test tubes and exposed to the light. It is found (Fig. 1) that all tubes containing gelatin with a pH $>$ 4.7 turn black in a few hours, while all the tubes containing gelatin with a pH $<$ 4.7 show no trace of darkening even when exposed to the light for weeks. The photograph (Fig. 1) was taken after an exposure to the light (often direct sunlight) for three weeks. It is, therefore, obvious that the silver gelatinate originally formed could only continue to exist for pH $>$ 4.7, i.e., on the alkaline side of the isoelectric point. A similar demonstration can be given when we substitute for the treatment with silver nitrate a treatment with neutral red or copper acetate, etc.

At the isoelectric point (pH = 4.7) the gelatin is insoluble and held in fine suspension. This is indicated by the fact that at this point the solution is opaque, while for pH $\gtrless$ 4.7 the gelatin is the more soluble the more the pH differs from 4.7.

If we return to our experiment it can be shown that in the non-blackened test tubes, i.e., on the acid side of the isoelectric point, the gelatin existed in the form of gelatin nitrate. This can be proved by the fact that if we bring the gelatin in different funnels to a different pH by treating it with a different concentration of HNO_3

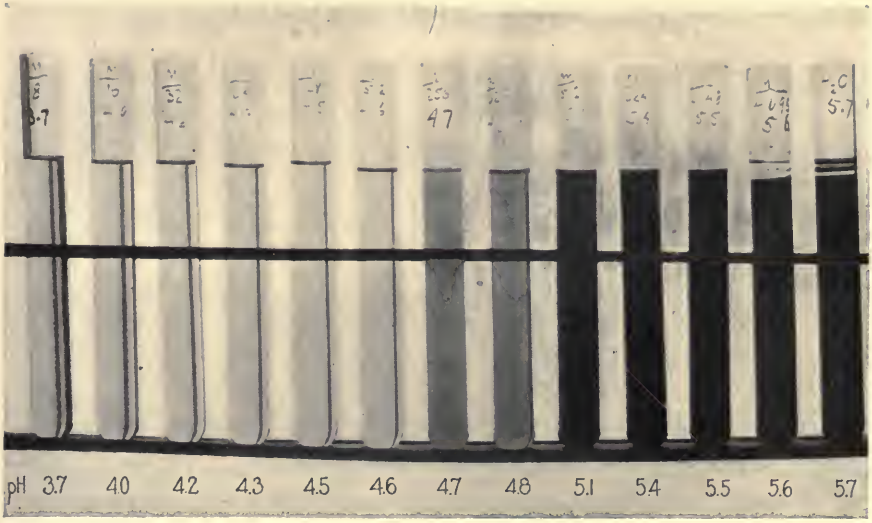

FIG. 1. PHOTOGRAPH OF GELATIN TREATED WITH SILVER NITRATE.

Each Test Tube Contains a 1 per cent Solution of Gelatin Which Had Previously Been Treated with M/16 Silver Nitrate, but was Brought afterwards to a Different pH by Treating it with HNO_3 of Different Concentrations and by Removing the Excess of Acid and of Silver Nitrate by Washing and Dialysis.

When these test tubes were exposed to light, all the gelatin with a pH > 4.8 turned black in a few hours, while none of the test tubes containing gelatin with a pH < 4.7 turned dark. This proves that the silver gelatinate gave off its silver as soon as pH became < 4.7. The photograph was taken after three weeks' exposure to light. The lower row of figures at the base of the figure gives the pH of the gelatin solution for each test tube, the upper row at the top of each test tube gives the concentration of acid used to bring the gelatin to the pH indicated. In one point the photograph is misleading, the gelatin solution with pH = 4.7 was white, but opaque, due to the fact that the gelatin at this point is insoluble at room temperature. The gelatin solution with pH = 4.8 was clear, but brown, indicating that it contained silver. While in the photograph tubes with pH = 4.7 and 4.8 look alike, they were in reality strikingly different.

in each funnel, and then after having washed off the excess of acid treat each gram of gelatin of different pH with the same rather high concentration (e.g., M/8) of a salt of Br or CNS, a volumetric analysis of the gelatin after the removal of the excess of the salt shows that Br or CNS exist in combination with gelatin only where pH < 4.7.

What is of greater significance, however, is the following fact: Pauli, (13) Ostwald, and other colloid chemists, have expressed a doubt that protein solutions can show a true osmotic pressure, and they are inclined to ascribe the "apparent" osmotic pressure to a "hydratation" of the gelatin. Since there are no measurements for "hydratation" it is impossible to put such speculations to a scientific test. Our method of using gelatin in powdered form and of washing away the excess of electrolyte after it has had a chance to act on the gelatin allowed us to furnish the molecular data necessary to prove that the osmotic pressure, swelling, viscosity, and other physical properties of gelatin are determined by the mass of gelatin salt formed. Figs. 2 and 3 show that the curves for the amount of swelling run approximately parallel to the curves representing the amount of Ag or Br in combination with the gelatin. The same was found to be true for the curves for osmotic pressure and viscosity. This leaves no doubt that it is the number of molecules of gelatin salt formed which determines the osmotic pressure —as the classical theory of van't Hoff demands.

The influence of electrolytes upon the physical properties of proteins can be accounted for on the assumption that gelatin (like proteins in general) is an amphoteric electrolyte which at the isoelectric point is practically insoluble while its salts are soluble; and under these conditions it is natural that the osmotic pressure should increase with the number of particles brought into solution. Procter (14) has developed an osmotic theory of swelling by acid according to which the quantity of gelatin salt formed under the influence of acid determines the swelling. This may explain why the curves for osmotic pressure and swelling of gelatin run parallel.

The hypothesis of the colloid chemists that the influence of electrolytes upon the swelling, viscosity, and the other properties of gelatin is due to a hydratation of gelatin ions becomes doubtful in the light of facts recently found by the author. Pauli and other

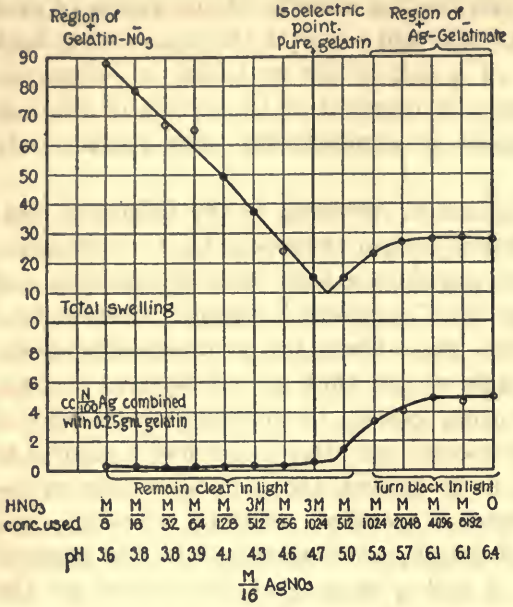

FIG. 2. Gelatin treated with different concentrations of HNO_3, from M/8 to M/8192, washed, and then treated with the same concentration of $AgNO_3$ (M/16), and then washed again. Abscissæ show concentrations of acid used. The final pH of the gelatin solution is found under the figure for the concentration of acid used.

The ordinates of the lower curve give the values for the silver found in combination with the gelatin. The curve shows that at the isoelectric point (pH = 4.7) and on the acid side of the isoelectric point, the gelatin was practically free from silver. On the more alkaline side the amount of silver found in combination with the gelatin increased with the pH. This proves that gelatin can combine with a cation only on the alkaline side from the isoelectric point, and this is corroborated by the fact that on the alkaline side from the isoelectric point only was the gelatin darkened by light. The ordinates of the upper curve are the values for the swelling of the same gelatin. On the alkaline side from the isoelectric point, where the gelatin had combined with silver, the curve for swelling runs parallel to the curve for silver gelatinate formed. It was, therefore, the relative mass of silver gelatinate formed which determined the physical properties of gelatin.

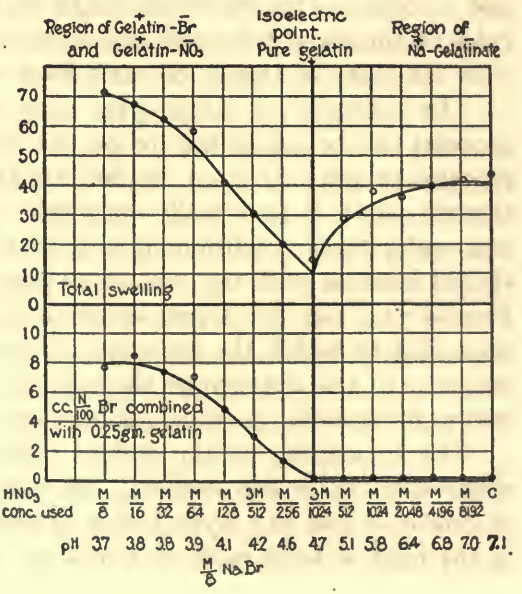

FIG. 3. Gelatin treated with different concentrations of HNO_3, washed, treated with M/8 NaBr, and washed again. The ordinates of the lower curve are the values of Br in combination with gelatin, showing that on the right (alkaline) side from the isoelectric point and at the isoelectric point gelatin contains no Br, while on the left, more acid side from the isoelectric point, the amount of the Br found increases with the pH. The ordinates of the upper curve represent the swelling of the same gelatin. The two curves on the left side are almost parallel, showing that the degree of swelling is determined by the relative mass of the gelatin bromide (or nitrate) formed.

colloid chemists assume that when protein is ionized it is surrounded by a jacket of water molecules, and the more protein molecules are ionized the greater this hydratation. The idea that ions in watery solution are surrounded by a water jacket the writer is not inclined to doubt. He questions, however, the correctness of the view that this hydratation determines the swelling, viscosity, and the osmotic pressure of gelatin. It is obvious that according to this hypothesis the swelling or osmotic pressure of gelatin should increase *ceteris paribus* with the increase of ionization. The colloid chemists who hold such a view have never put it to a test by measuring the conductivity of their protein solution, probably on account of the fact that with their method of investigating the effect of electrolytes on colloids in the presence of an excess of electrolyte this was very difficult. The writer's method of removing the excess of electrolytes after they had acted on the colloid permitted the measurements of conductivity necessary to test the hydratation hypothesis, with the unexpected result that the differences in conductivity which according to the colloidal hypotheses should exist are not found. The writer observed that gelatin salts with monovalent cation (Li, Na, K, NH_4) have an osmotic pressure about three times as great as gelatin salts in the same concentration with a bivalent cation, like Ca or Ba. The swelling and viscosity for these two types of gelatin salts yield curves similar to those of osmotic pressure. According to the colloidal hypothesis this would mean that the gelatin salts with monovalent cation are ionized three times, as much as the gelatin salts with bivalent cation of the same concentration. Measurements of the conductivity have shown that solutions of Li, Na, Ca, and Ba gelatinate of the same concentration have practically identical conductivity. This eliminates the colloidal hypothesis that osmotic pressure and swelling of gelatin are due to a hydratation of protein ions. On the basis of general chemistry a simple explanation for these facts is found on the assumption that calcium gelatinate forms molecules of the type Ca_2 $gelatin_4$, dissociating into three particles, two positively charged calcium ions and one aggregate of four gelatin ions with four negative charges; while sodium gelatinate dissociates into one positive Na and one negative gelatin ion. Eight particles of the latter will therefore carry as many charges as three particles of the former, which leads to a

ratio of osmotic pressures of 3 : 8 and a ratio of conductivity of 1 : 1, which were actually found. What is stated here for sodium and calcium gelatinate holds also for gelatin chloride and gelatin sulphate, their conductivities being alike, while their curves of swelling, osmotic pressure, and viscosity differ in a way similar to that between Na and Ca gelatinate. The hydratation hypothesis of swelling and osmotic pressure of colloids is therefore no longer tenable.

We thus see that the assumption of the non-validity of the laws of general chemistry for proteins (and other colloids) is not supported by fact. The error was due to the shortcomings of the methods used by colloid chemists in this work, two of which have been mentioned, namely, first the non-consideration of the hydrogen ion concentration of their solutions, and, second, the investigation of the proteins in the presence of an excess of electrolytes. The avoidance of these two sources of error has not only shown the validity of the laws of general chemistry for proteins but has also led to a simplification of protein chemistry.

BIBLIOGRAPHY

1. Arrhenius, S., "Immunochemistry," New York, 1907.
2. Langmuir, I., *J. Am. Chem. Soc.*, 1918, XL, 1361.
3. Oswald, Wo., "Die allgemeinen Kennzeichen der organisierten Substanz;" P. Hinneberg, "Die Kultur der Gegenwart, Allgemeine Biologie," Leipzig, 1915, p. 167.
4. Fischer, M. H., *J. Am. M. Ass.*, 1913, LX, 348.
5. Nasse, O., *Arch. f. d. ges. Physiol.*, 1869, II, 97; Loeb, J., *Arch. f. d. ges. Physiol.*, 1897–98, LXIX, 1.
6. Overton, E., *Arch. f. d. ges. Physiol.*, 1902, XCII, 115.
7. Höber, R., *Biol. Centralbl.*, 1911, XXXI, 575.
8. Loeb, J., *Science*, 1913, XXXVII, 430.
9. Hofmeister, F., *Arch. f. exper. Path. u. Pharmakol.*, 1891, XXVIII, 210.
10. Lillie, R. S., *Am. J. Physiol.*, 1907–8, XX, 127.
11. Loeb, J., *J. Gen. Physiol.*, 1918–19, I, 39, 237, 363, 483, 559.
12. Michaelis, L., "Die Wasserstoffionenkonzentration," Berlin, 1914.
13. Pauli, W., *Fortschr. naturwiss. Forschung*, 1912, IV, 245.
14. Procter, H. R., and Wilson, J. A., *J. Chem. Soc.*, 1916, CIX, 307; Procter and Burton, D., *J. Soc. Chem. Indust.*, 1916, XXXV.

A FEW THOUGHTS ON THE VIS MEDICATRIX NATURÆ

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THE fact that disease often tends to disappear, even when not treated, has only been a recent realisation in the history of medicine. It is, nevertheless, true that the Father of Medicine knew of it, as shown by his teachings that disease was, equally with life, a process governed by natural laws which indicated the spontaneous and normal direction of recovery, and by following which alone could the physician succeed.

"The healing power of nature was a Hippocratic doctrine. Not that Hippocrates taught, as he was afterwards reproached with teaching, that nature is sufficient for the cure of disease, for he held strongly the efficacy of art. But he recognised, at least in acute diseases, a natural process which the humours went through,—being first of all *crude*, then passing through *coction* or digestion, and finally being expelled by resolution or *crisis* through one of the natural channels of the body. The duty of the physician was to foresee these changes and to assist or not to hinder them; so that the sick man might conquer the disease, with the help of the physician." (Encycloped. Britann., XV., 800.)

Alas! that the profession in the succeeding centuries should have fallen so far from this simple doctrine.

From the earliest times until now, the theories of the origin and nature of diseases have varied greatly—at one time these were due to evil spirits; at another to various humours; at yet another to the influence of the heavenly bodies, and so on; but, while treatment always varied according to the prevailing theory, some treatment there always was, and when the patient recovered he was considered to have been cured by the treatment, and when he died then he did so in spite of it.

But, fortunately for medicine, some hundred and fifty years ago Hahnemann appeared. He condemned in no mild terms the heroic treatment of his day.

"The old school of medicine [sic], [he wrote] presupposes the existence sometimes of excess of blood (plethora—which is never present), sometimes of morbid matters and acridities, hence it taps off the life's blood and exerts itself either to clear away the imaginary morbid matter, or conducts it elsewhere (by emetics, purgatives, sialagogues, diaphoretics, diuretics, drawing plasters, setons, issues, etc.), in the vain belief that the disease will thereby be weakened and substantially eradicated; in face of which the patient's sufferings are thereby increased, and by such rather painful appliances the forces and nutritive juices, indispensable to the curative process, are abstracted from the organism. It assails the body with large doses of powerful medicines, often repeated in rapid succession for a long time, whose long-enduring and often frightful effects it knows not, and which it, purposely it would almost seem, makes unrecognisable by the co-mingling of several such unknown substances in one prescription, and by their long-continued employment it develops in the body new and often ineradicable medicinal diseases." (Hahnemann, "Organon of Medicine, vii.)

And a little later he writes:

"It is under the old physician who has been at last gradually convinced of the mischievous nature of the so-called art, after many years of misdeeds, and who only continues to treat the severest diseases with strawberry syrup mixed with plantain water (i.e., nothing) that the smallest number are injured and die."

If only Hahnemann had stopped here, what a new era he would have initiated! but, instead, he went on to propound a very fantastic theory of disease, so that he only endeavoured to replace the current theories (of plethora, morbid matters, and acridities) by another, equally unfounded in pathology. He passionately rejected, indeed, pathology and morbid anatomy, and believed only in "the derangements of the spiritual power that animates the human body." As regards treatment, he pressed his theory of *similia similibus curantur* (which had, indeed, been outlined by Haller, and by Tommasini, an Italian "contra-stimulist"). "He ascribed the effects of drugs to the spiritual power which lies hid in the inner nature of medicines," and, further, advocated the principle that the smaller the dose of these

medicines, the greater their power. Hahnemann was much persecuted on account of his views, but, nevertheless, had a great following, and by the introduction of these microscopic doses, he (all unwittingly) elaborated upon a large scale the experiment of seeing what happened in disease when it was uninterfered with by medicines. His results must have been much better than those of the "heroic" School,—better, indeed, than if he had given no medicine at all, for by the administration of his inert fractional doses, he would meet the craving of his patients for *some* treatment, and thus enlisted on his side the all-powerful influences of hope and faith. I say that he performed this great experiment into the power of nature to cure "unwittingly," for,

"It was a very essential part of his teaching that nature is a bad physician and not to be much trusted; that drugs are the real curative agents, provided by the beneficence of the Almighty." (Encyclop. Brit., XII, 128.)

Hahnemann's treatment was at least not actively harmful, and as he lived at the time when, as already said, the practice of giving enormous doses was all-prevalent, when the "stimulus" theory of John Brown and the "contra-stimulus" method of Rasori (copious bleeding and depressing remedies, such as antimony) held sway, it is small wonder that he had many followers. But, in spite of his work and writings, "heroic" therapy continued, and we have Joseph Bigelow writing sadly in 1860 (in his "Rational Medicine"):

"I sincerely believe that the unbiassed opinion of most medical men of some judgment and long experience is made up, that the amount of death and disaster in the world would be less, if all disease were left to itself, than it now is under the multiform, reckless and contradictory modes of practice, good and bad, with which practitioners of adverse denominations, carry on their differences at the expense of their patients."

As R. C. Ewing wrote in 1896 (*Med. Rec.*, June 13, 1896, 845),

"It was not until a much later period that physicians recognised that there is a something, and they know not what it is, aside from drugs, which plays an important rôle in the eradication of disease; and the highest minds of the present day are earnestly seeking a solution of the mystery. Have they found it, and can it be explained by the 'exhaustion' theory of Pasteur; the 'excretory' theory of Chauveau; the 'ozonised' theory of Traube; the 'tolerance of poisons' theory of Sternberg; the

'phagocytic' theory of Metchnikoff, or the 'immunising' theory of Vaughan? I shall let them answer,"

and although we can add several more theories since then, who can deny that the essential nature of immunity still remains to be settled?

But, as regards the question of treatment, we can at least now pride ourselves on the general recognition that there exist certain natural forces which tend to eradicate disease, apart from any medical treatment. Evidence of the natural tendency to recovery is everywhere seen in the vegetable and animal kingdoms. Generally speaking, the lower the organism in the scale of evolution, the greater and more complete is the tendency to restoration. A small twig, separated from the parent stem, will, when planted, grow into a new tree. If a *hydra* be cut in two, its basal end will grow a new mouth, and its oral end another pedicle. One limb of a star-fish can sometimes reform the whole animal. Going a little higher in the scale, a lizard, when it loses its tail, simply grows a new one, but the severed tail dies. A frog or a lobster similarly has a lost limb or claw restored. In mammals the reparative process is not so complete, but if a portion of the liver of a cat or dog be removed, it will be largely and quickly restored. Such are a few examples of nature's power of restoring tissues.

As regards function, the body has similarly great powers of adaptation to disturbance, as seen when one kidney will take on the function of both, and when in severe anæmia the yellow marrow of the long bones becomes red with its activity in producing red blood corpuscles.

The healing of an aseptic wound shews the natural forces all intent upon the restoration of the part. But when infection has occurred, then it is seen that the natural forces are not all upon the side of the sufferer. The tissues and body fluids are provided with certain powers of fighting the bacterial invaders, but the invaders are also provided by neutral nature with powers that help them. There are, from the patient's viewpoint, both good and bad forces of nature; it is only the former that constitute the *vis medicatrix naturæ*.

We may view Nature as the personification of the natural forces, and realise that she is neutral and would as lief that the man die as that he survive the infection. When a cancer becomes emplanted in the tissues, nature encourages its growth, and nothing but the

surgeon's interference will save the patient. In the same way, it is in accordance with nature's laws that a tapeworm flourishes in the intestine or the *acarus scabei* infects the skin. Both will continue indefinitely unless they are treated medicinally. Hence, while the physician must allow all natural forces that tend to help his patient to have full sway, it is often necessary for him to interfere with the course of nature, and here we see the limitations of purely "expectant" treatment.

Nature may be compared to an absolutely unbiassed judge, who dispenses the laws and exacts the penalties. And the laws are not human laws, but natural ones. A man poisons himself with alcohol, and the Court decides that he shall suffer and perhaps die. Another man shuts himself up in a bad atmosphere, and there, burning the midnight oil, wears himself out working, perhaps in order that his loved ones may live. But the verdict is that the tubercle bacilli, which, following natural laws, have emplanted themselves in his depressed tissues, shall win. The Court of nature is indeed one where natural laws are inexorably administered, but where sympathy and pity are unknown.

But the practitioner is not unbiassed, but wholly on the side of his patient. It is not an indifferent thing to him whether the cancer or the man win; whether the tubercle or the patient flourish. The alcoholic may have broken both natural and moral laws, but he must be saved, if possible, in spite of his natural and moral sins.

How, then, can the medical man best help his patient in his struggle back to health? In the first place, he must himself know the natural laws—the natural history of disease—just as a lawyer, in order to help his client, must know the laws of the country. Then he must needs instruct his patient (or better still the man before he becomes ill) as to the consequences of breaking the natural laws. Although all men must eventually die, how much life and needless suffering could be saved by the instruction of the public in the simplest laws of health—the prevention of disease rather than its treatment!

When a man becomes ill, his physician will place him in such surroundings that all the natural forces in his favour will have full scope. Rest, fresh air, and sunshine and nourishing food all help to raise the patient's resistance to infection and are opposed to the

infecting agents. Very often the medical man can increase the natural endeavours and thus help nature in the cure. A man breaks his leg, and nature will rest the limb by causing pain on movement. But the surgeon goes further, and by the application of splints increases the immobility and thus hastens the knitting of the bones. An individual swallows an irritant poison and nature causes him to vomit, but his cure will be hastened and made more complete by the timely use of an emetic or gastric lavage. Often the medical man must go still further. The cancer must be eradicated by the knife or it will inevitably grow until it causes death. An impacted gall stone or ureteral calculus may have to be removed, and so on. Tapeworms and many other parasites will persist unless they are removed by therapeutic means.

In other cases, for example in infections, the body tissues may win in the fight, unaided, but the physician can do much to sway the struggle in the right direction. Vaccines, by increasing active immunity, and antitoxins, by producing passive immunity, are examples here. In a few instances drugs will directly assist in the struggle, as in the case of mercury and arsenic in syphilis and quinine in malaria. But while some diseases can thus be treated specifically, the great majority of human ailments are yet beyond such satisfactory attack.

But the medical man's duty, and privilege, is not only to "cure" disease (or rather diseased persons), but also to relieve suffering. And it should, further, always be remembered that in relieving suffering, by giving the patient rest and ease, conserving his strength, we are doing more than this, we are helping the natural tendencies to cure—we are giving these forces time and opportunity to act. Who has not seen the whole aspect of a pneumonia patient changed for the better by a timely dose of morphia? The man has perhaps not slept for days and is nearly worn out, and his resistance almost gone, and then, following the opiate, he gets some hours of sleep and rest and thus is strong enough to reach his crisis. Nature has in time conferred upon him immunity, but he might not have reached this goal if he had not slept.

I remember many years ago seeing the good effects of a narcotic in the case of a pet dog. The animal had suffered so much from an irritating skin condition that it was reduced to skin and bone. In

family conclave it was decided to put it out of its suffering, and a huge dose of opium was given, and the poor beast was shut up in a coal cellar to die. Next morning he was found not to be dead, but to be sleeping heavily, and this went on for many hours. Then he awoke, peaceful and hungry, ate heartily, and in a week or two was well. The profound sleep gave him ease and nature did the rest.

One might enumerate many wearing symptoms, such as persistent insomnia, high fever, a trigeminal neuralgia, severe constipation or diarrhea, in which purely symptomatic treatment, where nothing more is found to be possible (or in addition to more radical therapy) may not only relieve suffering, but may go far towards helping nature to cure.

Symptomatic treatment is sometimes scoffed at (and rightly so, when anything more radical can be done), but very often it is all that is within our powers, and he is a bad physician, indeed, who does not then employ it. Even in mortal disease, such as inoperable cancer, surcease from pain and distress will often not only relieve the sufferer for the time being, but will actually prolong life for weeks or even months. In symptomatic therapy drugs are chiefly used; hydropathy is often of value here, but, after all, water is a pharmacopœial drug.

It has been well said that drugs sometimes cure, often relieve, and always console. We must remember that one of the most powerful influences towards a return to health is Hope. "What doctor," plaintively asks that delightful but highly-strung French writer, Amiel, "possesses such curative resources as are latent in a spark of happiness or a single ray of hope?" But it is surely one of the highest duties of the doctor to endeavour to inspire this hope, upon which so much of his success depends, not only in so-called "functional" conditions, but in organic disease itself.

He is a gruesome physician who tells his patient that no treatment will do him any good. In the first place it is not true. By this, it is not meant that we should always give medicines. Medical treatment is not necessarily medicinal, but includes every kind of physical, psychic, and other form of therapy.

As an old friend of mine expressed it: "There is more in Medicine than medicine!"

SOURCES OF INTELLECTUAL POWER

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QUESTIONS of the character suggested by the superscription inevitably come up when we consider the personality of our leaders. It is a problem of the highest human interest. Suggestions of it lurk in many discussions, and are embodied in most systems of education. Yet not often is there an attempt at direct answers. The subject can the more suitably be presented here, as the material on which it is based, though of general import, is largely of medical derivation.

There are of course many such sources. To say that they are covered by the biologist's formula of Heredity and Environment does not advance things materially. Whenever there is a rush of newer methods there is strong likelihood that older ones will be neglected if not prematurely discarded. And so often in medicine we see new achievements presently paralleled by improvements along former lines; in fortunate cases, then, each finds its own selective field or happily serves to complement the other. Something of this kind may hold for recent developments in psychology and genetics, and here certainly no aids, new or old, should be cast aside.

The proof of intellectual power is sought naturally at the top, not the bottom of the scale. As to what constitutes or is evidence of superior intellectual power opinions may differ. In the sense here intended it represents the highest expression of human thought and activity. There are many grades and nuances. Mere executive ability and acquisitiveness, for example, however useful qualities, are at times exhibited by animals in notable degree; and cannot consequently just of themselves be regarded as marks of high intellectuality. It is the later or superposed acquirements, racial and

personal, that can fairly be accounted the higher. Hence only the later or proximate Sources are here of concern, a selection of two of which will be briefly considered.

I. Medical Heredity as a Genetic Asset. A plan for estimating Sources that does not appear to have been applied may be called the Group or Epochal method. This permits a more exact determination in particular instances, and is in so far a scientific line of approach.

In this country, especially, great storehouses of possible material for study, collected for other purposes, it is true, are at hand in our libraries. It is the more in order to call attention to this, as the one we wish to honor has been such a valued supporter of our library system. This is a natural-experimental plan. So far as concerns the human side, that of chief and final importance to us, nature—in the guise of matings and progeny—is continually making experiments wholesale for us, if we but seek them out, and such as can never be equaled by those on animals. Our library files carry the protocols.

Two groups of epochal leaders with a common index will suffice for illustration.

(*a*). American neurology, aside from psychiatry, developed from the time of the Civil War. Half a dozen names will be recognized by those familiar with the facts, as embracing the main contingent of original contributors to that foundation. These were not only great as original workers, but they started a new discipline here, did a pioneer work, and, so far as concerns this country, created an epoch in their specialty, one of the most concrete developments in our medical history. The branch thus established can, moreover, claim a leading place on the intellectual side of medical work. If in such a group a common index can be made out, it must rank as a distinct and creative intellectual force. Such an index can be discerned by inspection of their line of descent.

There were others who did invaluable work, but these are the men whose contributions stand out.

1. S. Weir Mitchell, 1829–1914, first authority on nerve injuries, originator of the rest cure, b. Phila., son of John K. Mitchell, M.D. (1798–1858), grands. of Dr. Alexander Mitchell (1768–1804), and g. g. s. of a Scotch physician.

2. Edouard Seguin, 1812–80, authority on sub-mentals, and institutor of our first school for them, b. France, s. of Dr. T. O. Seguin, and g. s. of a physician.

3. Edward C. Seguin, 1843–98, first professor of neurology at P. & S., editor, well known for his contributions, b. France, s. of preceding.

4. Wm. A. Hammond, 1828–1900, author of first and long standard American work on neurology, original describer of athetosis, s. of Dr. John W. Hammond of Md.

5. Geo. M. Beard, 1839–83, an original describer of neurasthenia and general electrization, b. Conn., g. s. of Dr. Daniel Beard (1767–1815), g. g. s. of Dr. Spencer Field (1754–1801), and g.g.g.s. of Dr. John Frink (1731–1807). Beard's last call for "more light" may have come from theological inheritance.

6. John C. Dalton, 1825–89, author of the 3-vol. "Topographical Anatomy of the Brain," still the finest American work thereon, also "Physiology of the Cerebellum," b. Mass., s. of John C. Dalton, A.M., M.D. (1795–1863).

7. George Huntington, 1850–1916; his classic on the form of chorea known by his name was published in 1872; b. Long Island, s. of Geo. L. Huntington, M.D. (1811–81), and g.s. of Dr. Abel Huntington (1777–1858).

Reviewing this list it appears that six of the seven were sons of physicians while the seventh was descended from a line of physicians. Five were grandsons of physicians, and three were of even longer medical descent. It is clear that medical heredity was a strong feature of the group. Hence in addition to their own medical training we can look to their heredity in the same line, as the specific source of the intellectual force that produced an epochal result. Practically this holds whether effected through internal or external agencies. In fact, the analysis can be made more exact and incisive. The *character* of work undertaken by these men was, in accordance with their individual training, naturally directed to something in the medical field. But the *quality* of what they accomplished cannot be thus explained, as there were all about them plenty of others of medical training and some even interested in the same special subject, who failed to leave any comparable impress. Hence we must look further than to their personal calling for the source of their power, for a psychic gene which these men possessed in common and which was not possessed by the general run of their colleagues. This is supplied by the index of medical heredity.

(*b*). In an entirely different field of intense activity the writer found evidence of identical import. This was detailed in an article on "The Rôle of Physicians' Sons in the Lincoln Administration" (*Med. Rec.*, N. Y., 1916, October 28). There also seven men, nearest personally and officially to Lincoln in the work of his administration, who were all sons of men of medical rearing. They consequently present an index identical with that for the Neurologic group. These were Judge David Davis, John Hay, Hannibal Hamlin, Solomon Foot (Senate leader), William H. Seward, Edwin M. Stanton, and Schuyler Colfax, "next to Lincoln himself, the leaders in the executive and even the legislative work of the U. S. Government during that period."

These two groups, then, of quite unrelated character but with a common hereditary index, suffice to demonstrate "the superior intellectual value of medical training and heredity." Questions of selection of stock or of what other professions show do not affect the conclusion. Medical training can stand by itself as one of the highest sources of intellectual power in the offspring.

II. Varied Training as a Mental Activator. The general public has long been aware of this principle, and freely put it in practice in popular forms of instruction for after-life. Illustrations are so numerous and the evidence so generally accepted that proofs are unnecessary. The utilization, however, of this principle, its application in systematic development, falls far short of its possibilities:

The old adage, "A rolling stone gathers no moss," may hold in material and financial affairs, but the reverse is largely true as regards intellectual development.

It may be permissible here to take the course of our dedicatee for a text, as this gave him varied training and in sequence put him in touch with coming men in every leading country of the time. This source will also be shown by two illustrative types.

(*a*). *Double Professional Training.* This is a sporadic occurrence. Few students comparatively can afford the time and expense to take a second training, even in part; so that practically it is a self-limiting method. It is reviewed here, not as a plan for further exploitation (though that might be defensible), but as an illustration for this country how well one type of varied training works out in practice.

There is an old and wide prejudice against change of calling. And individuals who have enjoyed such opportunities are often difficult to trace after gaining distinction in the second line. Though apparently a cumbrous and inadequate plan, as about the only variation available with us in the past, its successes are the more in evidence. Illustrations in plenty might be adduced, a few types must suffice.

1. Mark Hopkins, M.D., S.T.D., 1802–87, president of Williams Coll. (1836–72).

2. Theodore D. Woolsey, D.D., LL.D., 1801–89, studied law and theology, president of Yale (1846–71).

3. William Harris, S.T.D., 1765–1829, studied theology and then medicine, president of Columbia Coll. (1811–29).

4. John M. Gregory, LL.D., 1822–98, studied law and theology, Mich. supt. education, president Kalamazoo Coll. and of Univ. Ill.

5. Roswell Park, D.D., 1807–69, West Pt. 1831, P. E. clergyman, prof. science Univ. Pa., president Racine Coll.

6. E. D. Warfield, D.D., 1861–, lawyer, clergyman, president Miami Univ. and Lafayette and Wilson Colls.

7. Newton D. Baker, M.D., 1871–, lawyer, U. S. Secretary of War.

8. Leonard Wood, M.D., LL.D., 1860–, Maj. Gen. and Chief of Staff, U. S. A.

9. James Wilkinson, M.D., 1757–1825, General-in-Chief, U. S. A.

10. William H. Harrison, 1773–1841, student of medicine, then gained military training, President of U. S.

11. Winfield Scott, 1786–1866, lawyer, Gen.-in-Chief, U. S. A.

12. Phil. Kearny, 1815–62, studied law, then a military course, Maj. Gen. U. S. A.

13. James A. Garfield, 1831–81, prof. languages and president Hiram Coll., lawyer, Maj. Gen. U. S. A., President U. S.

14. Montgomery Blair, 1813–83, West Pt. 1835, lawyer, U. S. Postmaster General (1861–64).

15. Richard Grant White, 1822–85, studied medicine, law, etc., author and critic.

16. Luther Jewett, A.B., M.D., 1772–1860, Congregational clergyman, editor, M.C. (Vt. 1815–17).

17. Lyman Abbott, D.D., LL.D., 1835–, lawyer, Congregational clergyman, editor of *Christian Union* and *The Outlook*.

18. Saml. F. Miller, M.D., 1816–90, lawyer, justice U. S. Supreme Ct., member 1877 U. S. Electoral Commission.

19. Thomas B. Butler, M.D., 1806–73, lawyer, chief justice Conn.

20. Paul Mumford, 1734–1805, physician, lawyer, chief justice R. I.

21. Jesse Root, LL.D., 1736–1822, clergyman, lawyer, chief justice Conn.

22. William Pinkney, LL.D., 1764–1822, studied medicine, then law, Atty. Gen. U. S., Minister to Engl. and Russia, U. S. Senator.

23. John F. Dillon, M.D., LL.D., 1831–, judge, prof. of law at Columbia, leading corporationist.

24. Launt Thompson, 1833–94, medical, then art student, sculptor.

25. J. McNeill Whistler, 1834–1903, West Pt. 1851–4, then artist.

26. William Thornton, 1761–1824, physician, first architect Capitol (D. C.)

27. Gen. Isaac Newton, 1837–84, student of medicine and engineering, famous at latter.

28. William Harkness, M.D., LL.D., 1837–1903, astronomer, prof. mathematics U. S. N., director U. S. Naval Observatory.

29. Geo. R. Dennis, M.D., 1822–82, graduate engineer, U. S. Senator, national delegate, R. R. president.

30. Wm. S. Haymond, M.D., 1825–85, graduate engineer, president I. D. & C. RR., M.C. (Ind. 1875–77), prof. and dean Ind. Med. Coll.

31. Joseph Thomas, A.B., M.D., 1811–91, lexicographer, prof. of Greek.

32. Francis Vinton, S.T.D., 1809–72, West Pt. 1830, lawyer, rect. Trinity, N. Y. C., prof. theology (P. E.)

33. Morgan Dix, D.D., 1827–1908, studied law, rector Trinity, N. Y. C.

34. Samuel Seabury, D.D., 1729–96, studied medicine, first P. E. bishop of Conn. and in U. S.

35. John T. Quintard, M.D., D.D., 1824–98, prof. physiol., later P. E. bishop.

36. Francis S. M. Chatard, M.D., D.D., 1834–1918, R. C. Bishop.

37. Wm. B. Stevens, M.D., D.D., 1813–87, P. E. bishop of Pa.

38. Edward Thompson, M.D., D.D., 1810–70, bishop, presdt. Ohio Wesl. Univ.

39. Isaac W. Wiley, M.D., D.D., 1825–84, editor, M. E. bishop.

40. George Upfold, M.D., 1796–1872, first P. E. bishop of Ind.

41. Matthew Simpson, M.D., D.D., 1811–84, M. E. bishop.

42. E. S. Janes, M.D., D.D., 1807–76, M. E. bishop.

43. Henry U. Onderdonk, M.D., D.D., 1789–1858, P. E. bishop of Pa.

44. Thomas A. Starkey, D.D., 1824–1903, civil engineer, P. E. bishop No. N. J.

45. Luther B. Wilson, M.D., D.D., 1856– , M.E. bishop, president Am. Anti-Saloon League, College trustee.

Many of the most distinguished of our early clergy had a medical as well as theological training, and hence can be cited collectively in illustration. And nearly all the more prominent medical missionaries, a long list, have also had a theological schooling.

The many medical men who in the past did so much in the sciences of chemistry, botany, and biology can be regarded either as doubly trained or as simply adopting an allied specialty. Geologists are, however, so far afield as to be illustrative of this form of double life. In the list are such names as, John S. Newberry, M.D., LL.D., 1822–92; T. Sterry Hunt, 1826–92, John Locke, M.D., 1792–1856; Wm. W. Mather, LL.D., 1804–59, West Pt. 1828; F. V. Hayden, M.D., LL.D., 1829–87; John Evans, M.D., 1812–61; Douglas Houghton, M.D., 1809–45; B. F. Shumard, M.D., 1820–69; Geo. G. Shumard, M.D., 1826–67; David Dale Owen, M.D., 1807–60; Richard Owen, M.D., LL.D., 1810–90; Chas. A. White, M.D., LL.D., 1826–1912; and three clergymen, O. W. Wright, A.M., M.D., 1824–88; J. P. Lesley, 1819–1903; Geo. F. Wright, D.D., LL.D., 1838–.

A side illustration to the same effect is afforded by the members of Congress who have taken both medical and legal training. To 1910 there were at least fifty such. Many of these were prominent in affairs both in and out of Congress. Considering there were relatively few in the country with such professional doubling, the number gaining this mark of favor is large enough to be notable.

Whatever may be the case in other countries, it is evident that in the U. S., from earliest time quite to the present, this form of education has yielded admirable results. That some of these men had a collegiate course as well, or other elements of inheritance or surroundings, does not affect the bearing of the facts shown. The medical may be the best primary or alternate training, though any excess of medical names in the lists is as much due to the kind of biographic material accessible.

The above is a sufficiently striking presentation, though only of a few names at hand. Its relative importance is enhanced many fold by the fact that this educational course has always been the exception. If, under such circumstances, and with strong prejudices to dispirit and oppose them, its votaries make so excellent a showing,

then we must conclude that their system of intellectual development has merit of a high order.

Clergymen, generals, lawyers and judges, educators, scientists, journalists, artists, are each represented. Hence clearly in all lines of intellectual importance (unless in that of imaginative[1] literature) the double scheme works out well. It is consequently of general worth as an intellectualizer.

It is evident that those of double training possess a binocular mentality, and a correspondingly superior perspective of life.

(*b*). *Migrations of Students.* Exchange of present or prospective calling is not practicable for the many. Training can be varied with success for far larger numbers, and by ways little used in this country. This involves well-tried and in no sense experimental methods.

This refers to students' freedom to take their professional course at more than one institution. Often there is only a transfer for a term or a year to gain instruction not satisfactorily given at the primary institution. Other objects play a rôle—to travel, enlarge acquaintance, compare methods and matters taught, learn opportunities, etc. But few of our student class get any timely understanding of the importance of this principle, and fewer yet are able to secure equable permission. Such applicants are eyed as shirkers of some sort. Accident and persistence may occasionally gain the chance. To the routinist this may seem but "climbing up some other way," that is merely because it is not customary. In America this practice has had little vogue. But in some countries it has been used so long and so largely that its merits are beyond question. Possibly it has not been favored here because it costs nothing; and as it carries no reward there is no profit in advancing it.

No one who has not had experience with the habit of student migration can have any appreciation of its peculiar and rounding usefulness for the student himself, and the healthy stimulus it gives to teachers as well. It is one of the few great principles that have given such impetus to teaching in the lands where practiced, though rarely considered in discussions by our educators.

[1] In the case of fictionists variation, similar to that above seen in formal education, may be of other origin, as from travel, personal experience, or inheritance. Someone has shown that poets are of mixed racial stock, thus establishing for them an analogous equivalent due to heredity.

As a recent writer says: "The faculties of our universities are undoubtedly too immobile."[2] Change his word, "faculties" to read "students," and it applies here. To make faculties move or mix involves vast trouble; students will move themselves, if freely permitted.

Exchange professorships are fine courtesies and have a place. But, as occupants with technical outfits can hardly carry everything with them, it is not an exchange in any full sense, and must be limited either to those not so encumbered or be but a special performance. However valuable, the scheme does not give much added scope or choice for students.

On the other hand, the principle of exchange can be extended to all students. There might even be exchange-studentships. For scholar and professor alike it is good to have an open chance, information as to how to work out his own salvation, and the prospect of gaining a meed of recognition.

No medical man in the recent annals of this country has been so keen to award recognition to both friend and stranger as the dedicatee of this work, one of his little-noted services to American medicine. Some scheme is certainly desirable for animating students who *en masse* too often feel like "dumb driven cattle."

Elective courses do not offer much variety in the present sense, nor can they find a ready place in professional schools.

Neither is it met by scholarships, fellowships, or other stipends, barring the traveling kind. At most these are for the few, and afford no solution for the great body of students. And, regarding the selected holders of these billets, the Biblical adjuration about the stone that the builders rejected is, as every observer well knows, quite as true now as in early times.

The development of graduate opportunities offers a solution, though belated as regards the individual, and only for such as can afford more extended study. If the present talk of economy applies to education, here is a chance by better use of undergraduate time. For any adequate plan adapted to general needs we can consequently but come back to that of student migrations as the best, the fairest that the world has so far devised. The change privilege might be given as a reward to those above a certain

[2] Nutting, in *Science*, 1918, December 20.

standard of scholarship, were it not that the laggard is the one most in need of stimulus.

In no case, as it works out in practice, are a majority of the students ever at one time away from their favorite institution. And those who stay at one place for their whole course get benefit by association with those who do make use of the privilege; information is continually exchanged with those from other seats. For its patrons it insures a more intimate acquaintance with each center and its student-life than does either of the substitute propositions. It adds in all these ways greatly to the intellectual progress of the whole student body. The long distances that many of our students have to travel to reach their professional schools would not be materially affected by such modification of custom. The remoteness of many such institutions from one another may oftener be a handicap, but would make little difference to the enthusiasm of our youth.

To account for this lack of opportunity with us, there is of course a shift of reasons. It is said by some of our university men that any such freedom is incompatible with the American system—simply a form of gentle evasion. Another time it is claimed that only a strongly centralized power can do anything—also to be taken with allowance, as any State or school can start the work for itself and accomplish something.

The lethargy of a petrified relic comes nearer to the real reason. In the early years of all our professional schools, as soon as a student matriculated he was viewed as a financial resource. This old way of regarding students, and as a result their habits of procedure, still persists. In fact all the schools continue to find a use for their student fees, and where this necessity is at all relaxed there comes the desire for its prestige to score as big a roster of students as possible. Consequently former ideas and customs still hold sway. In fact, without some degree of enlightenment as to the value and uses of the privilege, loosening the strings might have little more effect on our students than lifting the bars about long-caged animals. Time would serve to correct this.

It can be realized in one of two ways. Any school can offer permission to its students, merely requiring satisfactory certification of study elsewhere. In a sense this is now possible, but the impedi-

ments everywhere placed in the way are so troublesome, and co-operation, or practically unionism, is applied with such effect that rarely does a student attempt change, unless compelled by circumstances.

The other plan must await the extension of inter-collegiate examining work from the present entrance tests to the later stages of training. When that extension of university methods is realized, this desideratum may find its natural fulfillment. There will still remain the wider ideal of its extension between accredited nations.

What objections? None that is valid. Migrations do not interfere with systematic study or teaching. Students can remain at any preferred place, and graduate where they like. This involves no outlay by institutions, nor does it lengthen the time of study.

The only apparent criticisms are: Possibly a slight amount of clerical trouble in giving certificates for work accomplished. And an imaginary loosening of alumni attachment. In practice this latter does not seem to materialize. Either the present system chafes many excellent students, or for whatever reason the attachment of a goodly proportion of our alumni ceases at graduation. By the liberal system a deeper appreciation of the educational parent is often engendered. The balance is rather in favor of migratory permission,—better trained, better satisfied, and hence more devoted and more available graduates.

The advantages of student migration include such matters as:

1. Enlarged acquaintance with conditions, teachers and fellow-students, especially those who are to be future colleagues in life.

2. A rounding out of studies by choice of opportunities.

3. Greater variety in social experience and in training, with relief of the narrowness so common at single schools.

4. The enormous stimulus to and broadening of the teachers themselves.

5. The bringing back of added spirit and of common information, in the usual cases of return to the former place, or by new students from other places.

The value of variation in mental training, as an aid to intellectual development, can be traced in many directions, though not often with any degree of exactness if even of certainty. To attempt this, two definite and determinable types have here been considered. These

are so similar in character that the first or larger (educationally, not numerically) includes the second or smaller; and the latter rests on its own basis as well.

Of the two sources outlined, it is not necessary for present purposes to decide whether the former is due to inheritance of acquired characteristics, to the gradual accumulation of family tradition, education, and opportunities, or to other technical cause. The pragmatic conclusion holds, that medical heredity is one of the best sources. Like most hereditary factors in the human, it can hardly be made of direct use, but may have the more theoretical and historical interest.

The second source, on the contrary, adds little on the side of theory, but, like all environmental elements, offers something available, and carries with it its own lessons for students themselves and their sponsors.

THE PSYCHOLOGY OF ANTICIPATION AND OF DREAMS

By Frederick Peterson, M.D., New York

THE thread of thought, the train of ideas, the stream of consciousness, are familiar phrases in psychology. On the thread of thought are strung the past, the present, and the future. On the train of ideas we leave one coast behind for the coast that lies far ahead. The stream of consciousness flows from the reservoir of memory across the present into the unknown to some distant sea.

The books on psychology tell us much of memory and of the action of mind in the present, of volition, attention, judgment, emotion, association, concepts, instinct, perceptions, but they tell us very little of the relation of that stream of consciousness to the future. Nevertheless, the essential function of the mind is its dealing with the future. Anticipation of the future is the light that guides our conduct, which plans and chooses, which distinguishes the right from the wrong paths that we are to follow, and the ways that are favorable to progress from those that are unfavorable. Our memories are our experience, the present is a point, the future is everything. In youth especially the preoccupation of the mind is almost wholly with what is to come. In old age which has no future the predilection is for the past. Childhood and adolescence are one long preparation for the future, groping, seeking, planning, foreseeing. The education of our young people is not so much a drawing out of latent faculties as a filling in of the mind with the kind of knowledge and experience that shall determine future conduct, foreshadow the events that are to be, choose the best in ambition and endeavor.

It is not that the future in mental function is so much concerned with prophecy, augury, premonition, presentiment, soothsaying, clairvoyance, horoscopes, or even astronomical prediction, but that it enters into the very psychology of our everyday life. This is abundantly shown by the richness of language in words involving the element of futurity, such as foreboding, forethought, foreordain, forecast, forewarn, foresight, foretaste, foreknown, presage, predisposition, prevision, provision, providence, prospect, prescience, pre-

determine, premeditate, divination, auspices. These are some of many markedly futuristic words, but the same element of futurity is present in countless other words, such as expect, intention, speculation, design, resolve, plan, provide, problem, solution, preparation, rehearse, discern, training, evolve, surmise, prudence, sagacity, deliberation, counsel, fate, advise, promise, calculation, announce, explore, menace, likelihood, curiosity, destiny, and the like.

All of our hopes, desires, wishes, drives, trends, tendencies, propensities, needs, longings, cravings, ambitions, and aspirations—as well as our timidities, anxieties, suspense, surprise, dreads, and fears—have to do with this same element of anticipation. Yet the academic psychologies scarcely mention the future with the exception of an occasional paragraph on expectant attention. We have need now of a new study of the psychology of anticipation.

The sculptor prefigures in the block of marble some divine creation. The painter with his palette of colors and stretch of canvas foresees the whole to which laborious days will bring fruition. The speculator and politician devise their schemes for success on well-laid plans for the far-distant future. The whole life of the growing child is preparation for the work of life, with days full of joyous anticipations of pleasures to come, laying in stores for future use, and hours sometimes tinged with little worries over the future, or with apprehensions for misdeeds punishable by parent or teacher, or with occasional fears born of reprimand, or of unwholesome stories. The stream of consciousness in the scientist busied with some burning problem stretches far out into the unknown yet surmised beyond. What vast horizons beckon to the philosopher who reaches with his antennæ of ideas into the void of space and coming time! Even I, who occupy my days with patients, busy myself with their hopes and fears and with the prognosis, and among my recreations watch with expectant attention my growing crops and increasing flock of Dorsets; while on journeys to and from the farm I read detective stories, planned by expert writers to keep me always in the condition of alert anticipation as to what comes next. Every novelist writes for the anticipation of his readers, and every reader is leaping forward to the climax of the story with his faculty of expectation. When the gifted orator on the platform is expounding his experience or solving his problem, the attentive listener not

only follows his line of argument, but pushes forward to the culmination often before the speaker gets there himself. In an extemporaneous address, especially if given in a foreign language, in which one is not altogether fluent, the speaker's own thoughts as well as those of his hearers are always running ahead of his laborious expression. In listening to music, the mind of the listener is constantly anticipating the coming changes of harmony, the return of phrase and motif. The fears, suspicions, anxiety, hopelessness of many morbid mental states are in reality a disorder of the faculty of anticipation.

Now since we live in a world of common sense and practical realities, let us see how this view of the stream of consciousness applies to dreams, which, grotesque and bizarre as they generally are, still belong to our world of realities, even if a sort of underworld of realities.

Bergson compares our store of memories to a pyramid whose point is inserted precisely into our present action. We might perhaps compare the mind to a fountain pen filled with experience, with its point of the present poised and ready to write upon the white tablet of the future.

In conscious and directed thought we draw upon a very limited store of memories, but dreams often seem to release and use the whole. The day dream, the undirected stream of thought, the idle drift of fancy or phantasy, with its relaxation of control, lies between directed thought and dream, and is usually concerned with pleasant anticipation or agreeable reminiscence in a comfortable state of mind and body. (There is little day dreaming among those suffering from physical distress or care, worry, and anxiety.)

Even the concentration of directed thought is subject to intrusions of more or less irrelevant fringes of other chains of associations or occasional saltatory ideas. In day dreams the looseness of concatenation lends itself still more to such intrusion and incoherence. In the dreams of sleep there is still greater relaxation of direction, all the doors of memory are unlocked, flung wide, the countless strands of associations are rewoven in kaleidoscopic patterns, with all sorts of intrusions, auto-suggestions, and immediate suggestions from the more or less active sensory apparatus of the body, all played with by reminiscence and anticipation. The antici-

pations may be disagreeable and painful or agreeable and pleasant, and the dreams correspondently occupied with subjects of apprehension, fear and terror, or of hopes, wishes, and desires. The currents of dream consciousness would seem to be a kind of reflection of the currents of alert consciousness, a moonlit underworld of daily common life, with wider horizons as to past and future, without the tension of directing and choosing, though not wholly "disinterested," as Bergson would have it, with a looser mesh of association, and wide open to suggestion from any source, either in the flowing stream of the unconscious mind or in the sensitive body that houses the mind.

One of the amazing features of dreams to many is the tendency to tell a story, to dramatize, or even as in the case of Coleridge to write a complete poem (Kublai Khan). Robert Louis Stevenson, in his "Chapter on Dreams," gives us a very good picture of the child with night-terrors and nightmares made up for the most part of a confounding of his everyday school troubles and tasks with the "ultimate and airy troubles of hell and judgment," which later grew with his dawning outlook on the great world and his increasing knowledge and aspirations into quiet anticipatory dreams of journeys to strange towns and beautiful places with adventures; and presently he began making stories in his dreams; and later to write them out and sell them like the thrifty Scotchman that he was.

Dramatization in dreams is probably not unusual, and depends upon that same anticipatory faculty which leads the novelist on with his story and his reader to go far in advance of the novelist's pages. A thought, a sensation, a picture, or a sound in the dreamer starts up an anticipatory idea and this another until the plot is woven. On a steamer coming home from China I suddenly woke one night and wrote down at once this nonsense jingle that I had just dreamed:

Said Zambo-Ango
"Where is my bango?"
And Whango said
"I am."
Said Zambo-Ango
"You rotten mango
I'll kick you to Siam."
And Whango said
"Go damn."

I had probably seen the rather amusing name of the town Zamboanga on a map of the Philippines, and with a tendency to rhyming, the word in the dream suggested by anticipation one rhyme and idea after the other in the order quoted. Of course the anticipatory faculty would be nothing without memories and experience. These are naturally drawn upon for the development of the projected sequence. How this is accomplished and why dreams exhibit often so much incongruity and incoherence is well presented by Bergson. Suppose there should arise in the visual field of the dreamer a green spot with white points. Very different memories might be summoned by this sensation—a lawn with white flowers or a billiard table with balls or a host of other things besides, and one of these may pass into the other. I recently had an experience of this kind. I went to sleep on a sofa looking into a round mass of red embers in the fireplace. I dreamed a dog was coming toward me with one great blazing red eye. At first, a little alarmed, I remembered it must be my Airedale asleep on the rug by the fire. Immediately a bare arm appeared before me with a round fresh vaccination mark, bleeding. Both dreams were evidently based upon visual after-images of the heap of glowing coals.

Anticipation utilizes the material of past experience much as is done in the construction of the cantilever bridge, where suitable material is brought up piece by piece, fragment by fragment, from behind and pushed forward and fitted into the extending arch until the whole aerial span is finished. When dreams are dramatized there is no failure of interest in the plot. It is not quite a "disinterested" process.

In recent years much has been published on the Freud theory of dreams. It would seem that Freud in meditating on the unconscious was much struck with the dreams of his children, which doubtless were busied chiefly with joyous anticipations of days in the country, trips to the Prater, toys, theaters, jollifications, and it quite naturally occurred to him in this connection that some dreams might be the "fulfillment of a wish." It was a saltatory idea that took complete possession of him, and before long he announced in a book the hypothesis that all dreams are "the fulfillment of a wish." Every dream henceforth had to be interpreted in accord with his anticipatory desire to find a wish-fulfillment.

The difficulties proved very great, but if one is sincerely bent upon discovering ciphers in Shakespeare there is always some Ignatius Donnelly to do it. As so many dreams present painful or distressing contents, fears, and so on, among their anticipations, reflecting the tendencies of normal waking thought, it was necessary to invent something entirely new and quite at variance with usual conscious thought processes to support the Freudian preconception. If after reading his book you have a fear dream, the concealed wish is very clear as a desire to confute Freud. (He gives instances of this in his book.) When the wish is not as manifest as this, one has recourse to the "latent dream content" with such remarkable "distortion" and "displacement" that only Freud and his followers can interpret it properly. The "dream censor" is evoked with his unpleasant faculty of "disfiguring" or "disguising" the dream-contents in order to conceal the real wish of the dreamer from any but the analyst. Thus the formula for the interpretation of fear and anxiety dreams, which by common-sense explanation would simply reflect in a measure such fears and anxieties as we often have in our conscious life, is to quote Freud. Such dreams are "the disguised fulfillment of a suppressed or repressed wish," and "the content of fear and anxiety dreams is of a sexual nature, the libido belonging to which content has been transformed into fear."

A neurotic young lady, a patient of mine, often has a fear dream as follows: She dreams she is awakened by the house being on fire and she runs from the house in a panic scantily attired. A Freudian interpretation would be easy and clear—and yet very far from the fact. On two occasions the country houses in which she lived did actually catch fire in the night and burn to the ground, and she ran from the house on each occasion in a state of panic scantily clothed.

The extraordinary symbolism ascribed to dream-life by the "new psychology" is chiefly the invention of the psychanalysts. There is probably little in the subconscious or unconscious mind of any individual that has not at some time been conscious, and there can be no symbols there which have not been at some time symbols in waking thought. Most of the symbolism described by the new interpreters of dreams reflects the symbolism of the analysts themselves. In fact there is more to be learned from the interpretations published of the psychology of the analyst than of the psychology of

the dreamer. The analyst reveals himself in his analysis, his anticipations, his intelligence, his learning, his logic, and his wish, for if there is any wish brought clearly to light in the analysis it is that of the interpreter; and the theoretical "distortion," "displacement," and "disfigurement" ascribed to dreams in "the new psychology" become actualities in the analytic story.

To the Freudian there is but one drive, the sexual, and to him all the arts and accomplishments of civilization are but the sublimation of that. This is a Rabelaisian theory. It will be remembered that Pantagruel in his travels met one Gaster by name, who considered all the powers and attainments of man to be the sublimation of the desires of the stomach.

In reality there are many powerful drives besides those of sex and hunger, well described by Woodworth in his "Dynamic Psychology," among which may be mentioned fear, disgust, curiosity, anger, self-assertion, submission, the gregarious instinct, the instincts of construction and acquisition, imitation, suggestibility, play-instinct, and all the later acquired drives determined by special gifts and aptitudes in the great workshop of the world, and our absorption in our particular interests there. Individual development is one long series of "preparatory" or anticipatory reactions for the "consummatory" reactions that are to follow. It would seem as though sex and hunger play a secondary part in the behavior of mankind in general. Survival and reproduction are necessary to man's advance as conqueror of his environment, but the goal of his ultimate consummatory reaction is the encompassing by his brain and mind of the planet and the stars.

What has been said of the faculty of anticipation in our mental processes is in a measure paralleled in our physiological and morphological makeup. Sherrington has pointed out how the special sensory apparatus of the "leading segments," the "distance-receptors" (nose, eyes, ears) in biological evolution, have contributed most to the uprearing of the cerebrum, extending the powers of investigating the environment, projecting the creature into wider horizons.

Feeding and reproduction, necessary but subsidiary functions of our being, are relegated to the lower segmental levels. In the leading segments lie these sensory distance-receptors which have made possible the anticipating, curious, and exploring mind, eager to know and dominate the universe.

CLINICAL AND DEVELOPMENTAL STUDY OF A CASE OF RUPTURED ANEURYSM OF THE RIGHT ANTERIOR AORTIC SINUS OF VALSALVA

LEADING TO COMMUNICATION BETWEEN THE AORTA AND BASE OF THE RIGHT VENTRICLE, DIAGNOSED DURING LIFE. OPENING IN ANTERIOR INTERVENTRICULAR SEPTUM (PROBABLY BULBAR SEPTAL DEFECT). MALIGNANT ENDOCARDITIS[1]

By Maude E. Abbott, B.A., M.D.,

Curator of the Medical Museums, McGill University, Montreal

(From the medical wards of the Royal Victoria Hospital)

ABNORMAL communications between the aorta and base of the right ventricle, or between aorta and pulmonary artery, are of not very infrequent occurrence. The event is accompanied in the great majority of cases by characteristic symptoms, and signs so striking as to be pathognomonic. In a few of the cases the communication is of congenital origin, and the clinical evidences of its presence have existed throughout life; but in far the greater number it is formed by the sudden bursting of an aneurysm of the base of the aorta into the pulmonic circulation, and symptoms then set in suddenly. Such aneurysms may be of the so-called "spontaneous" type, in which the wall of the ascending aorta is extensively diseased, from luetic or other causes. There is, however, an extremely interesting group of cases in which the aortic wall is perfectly healthy, and the right anterior aortic sinus of Valsalva is the seat of an opening leading into a finger or thimble-like process which projects into the conus of the right ventricle and represents an aneurysm of its wall and that of the aortic sinus, due not to disease, but apparently to a congenital thinning of the septum between the two great trunks. This was evidently so, and is the explanation put forward in the cases of Beck, (1) Hale-White, (2) Krzywicki, (3) and Kraus, (4) in which the walls of the aneurysm

[1] The anatomical portion of the study of this case was made under a grant from the Cooper Fund for Medical Research.

were thin and membranous, without sign of inflammatory action of any kind, and rupture had taken place at the apex of the sac, evidently as a result of strain. In the case of Krzywicki the ventricular septum was entire, but in the other three above cited, and in several similar ones in the literature (Hart,(5) Thurnam,(6)) in which the conditions were obscured (as in our own case) by the existence of a malignant endocarditis, the aneurysm of the right aortic sinus was associated with a defect of the anterior interventricular septum immediately below the cusp, in a situation identical with that of the interventricular communication in the case which it is our privilege to report here, and both conditions were ascribed by those who recorded them to a defective development of the aortic (bulbar) septum at this point.

The clinical features of abnormal communications between the aorta and pulmonary circulation were clearly outlined by Thurnam (6) in 1840, who reported 1 case of ruptured right aortic sinus aneurysm (summarized below), and mentioned 5 others within his knowledge in which a thin-walled membranous sac projected into the right ventricle, but was not ruptured; by Peacock (7) in 1868, who included Thurnam's series in a review of 17 cases from the literature, and by Brocq (8) in 1886. In all the cases except 4 cited by these authors the communication was "accidental," due to rupture of a "spontaneous" aneurysm of a diseased aortic wall; of the other 4, which were all believed to be of congenital origin, 2, 1 by Thurnam, (6) and 1 by Rickards, (9) were cases respectively of ruptured aneurysm of the right aortic sinus, and congenital opening in this situation. In the other two by Wilks, (10) and Baginsky, (11) a smooth-walled aperture of communication between the aortic and pulmonary trunks lies above the valves but below the origin of the innominate artery (thus excluding patent ductus), and represents a defect at the upper part of the aortic septum. (See Plate IV, S. a. p.) Similar cases of congenital perforation at this point above the valves were reported by Fräntzel, (12) 1868, Girard, (13) 1895, and Hektoen, (14) 1900, who adds a valuable developmental study of aortico-pulmonary communications of congenital origin. He quotes a case by Charteris (15) of much interest in relation to the subject of this article, in which a hole behind the right aortic cusp leads directly into the base of the right ventricle without any sign of aneurysm or inflammatory action, evi-

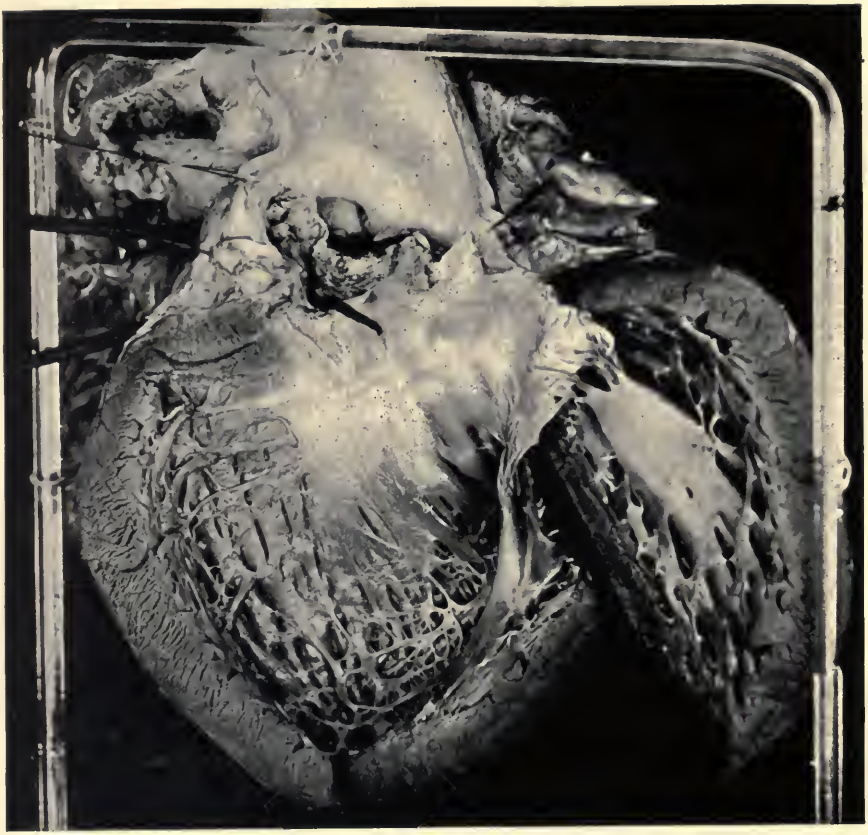

FIG. 1. ANEURYSM OF RIGHT AORTIC SINUS OF VALSALVA, RUPTURING INTO RIGHT VENTRICLE AT LEVEL OF PULMONARY VALVES.

Associated with Opening in Anterior Part of Interventricular Septum Leading into Conus Arteriosus of Right Ventricle (probably Bulbar Septal Defect). Malignant Endocarditis of Aortic and Pulmonary Valves and Adjacent Endocardium. View from Left Ventricle.

The Aortic Cusps are seen Thickened and Deformed by Old Endocarditis and Surmounted by Recent Vegetations with Ulceration of Subjacent Myocardium. Two Probes are Passed, the Upper through the Opening in the Right Aortic Sinus, the Lower through the Interventricular Communication Immediately below the Cusp, and are Both Seen Emerging Close Together in the Conus Arteriosus of the Right Ventricle. The Interventricular Communication is Seen to Lie in the Anterior Part of the Septum Some Distance in Front of the Pars Membranacea, and Directly below the Anterior Half of the Right Aortic Cusp in the Extreme Anterior (Bulbar) Part of the Interventricular Septum. From the case here reported.

dencing a true defect at this point and not merely a congenital thinning. Rickards (9) reported a similar opening combined with ventricular septal defect (summarized below).[2]

The characteristic clinical picture presented may be summarized as follows: Dyspnœa without cyanosis, precordial vibration and thrill of intense purring character, and loud sawing murmur, sometimes systolic, sometimes diastolic, but usually continuous, with systolic or diastolic accentuation, and synchronous with the thrill. These signs are differentiated from those of patent ductus by their extremely superficial character relatively to the chest wall, and by their point of maximum intensity being definitely at the base of the heart and over the middle of the precordium. In the very rare cases of congenital perforation of the trunks (Wilks, Baginsky, Fräntzel, Girard, Hektoen) or of the right aortic sinus (Charteris, Rickards), these signs were of course persistent throughout life. In the far commoner ones of ruptured aneurysm, a sudden onset in a person in apparently perfect health is a part of the symptom-complex. The patient may survive the rupture for years, the precordial thrill and murmur persisting unchanged.

The following case, which presents a picture pathognomonic in all details of an aneurysm of the base of the aorta rupturing into the pulmonary artery or base of the right ventricle nine years before death, occurred in the public service of Dr. W. F. Hamilton, who kindly accorded to me the fullest privileges of observation during the nine months of the patient's stay in the hospital, and gave me the opportunity of making the ante-mortem diagnosis. The clinical notes were made by Dr. C. R. Joyce, house-physician in charge, with my own collaboration.

Case. G. R., Englishman, aged thirty-six, intelligence above the average, never had chorea, rheumatism, or venereal disease, and had never used tobacco or alcohol. Admitted to the Royal Victoria Hospital, Montreal, on October 27, 1914, immediately upon his arrival in Canada from England, being referred by the Immigration authorities on account of his cardiac condition. Complained of slight dyspnœa, weakness, and sense of pulsation in the temples. Gave a history of having been in apparently perfect health, and leading a strenuous life following his trade

[2] Good examples of so-called "spontaneous" aneurysms rupturing into the pulmonic circulation with life maintained for some time are the cases by Roberts (20) and Gairdner (21).

as a carpenter, and also working as a Methodist preacher, until the age of twenty-seven, when he suddenly became aware of a feeling of cardiac irregularity and of throbbing in the temples. He took to bed under medical advice, and a month later was admitted unimproved to the Grantham Hospital, Surrey, England, where he remained in bed for nine months. Here *the diagnosis of aneurysm* was made and *the intense precordial vibration,* which is perfectly evident to his own senses, *is stated by him to have been first noted.* After his discharge he remained in bed at home for fifteen months longer, when the signs of cardiac insufficiency passed off, and he was able from this time until his sailing from England to follow his work as a Methodist preacher (though not his trade as a carpenter), without subjective symptoms. *The precordial vibration, however, had persisted to the present time.* He was extremely seasick on shipboard.

Examination showed a tall, spare, poorly nourished man, of flabby musculature, dyspnœic on exertion, without cyanosis, clubbing, or œdema. Posterior cervical, sub-maxillary, and axillary glands slightly enlarged. Marked pyorrhœa alveolaris. Temperature 100°, remittent type. Wassermann negative, hæmoglobin 65 per cent, R.B.C. 3,230,000, W.B.C. 12,300. Pulse 84, waterhammer. Marked pulsation in temples and vessels of neck. Capillary pulse.

Heart. Slight precordial bulging and widely distributed heaving impulse over whole precordium. Apex beat visible, precordial vibration and *very strong diastolic, almost continuous, thrill,* felt over the precordium, of *maximum intensity in second and third left interspaces,* where it is so strong that a vibration may be felt when the fingers are held half an inch away from the chest. This thrill is transmitted to the right nipple line, below to the seventh rib, above to the clavicle, and to the left to the midaxillary line. Slight presystolic thrill at apex, and systolic thrill in vessels of neck. Heart dullness at second space, 3½ cm. to right and 15½ cm. to left of midsternal line. At apex systolic and diastolic murmurs, transmitted to posterior axillary line, and a rough presystolic murmur. At the base a *very loud rough diastolic murmur almost continuous, being interrupted for only a brief time in systole with maximum intensity in third left interspace. This murmur is extremely superficial and may be heard with the ear 2 inches from the chest wall.* Another rough systolic murmur is heard best over pulmonary cartilage. To-and-fro murmurs behind from apex of left lung to level of fifth dorsal spine.

During the succeeding months the temperature became high and of septic type (98° to 105°), with occasional severe chills. Blood cultures on November 10th and December 21st negative. Weakness and dyspnœa became progressively worse, vomiting set in, albuminuria, hæmaturia,

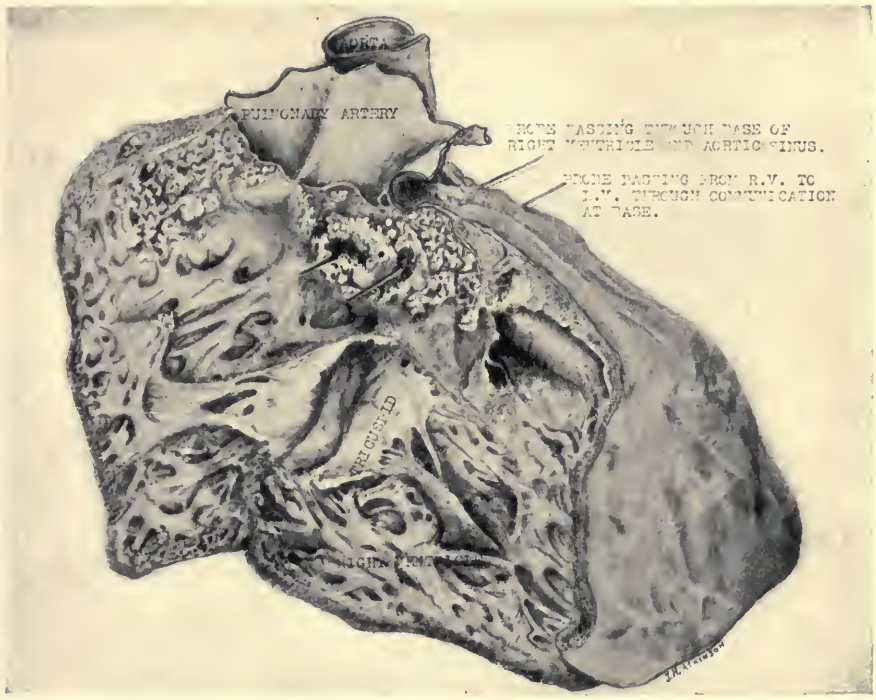

FIG. 2. VIEW FROM RIGHT VENTRICLE OF THE CASE SEEN IN FIG. 1.

Showing Probes passing through (*a*) Trumpet-Shaped Tube,* in the picture, Fringed with Vegetations (the Ruptured Aneurysm of the Sinus Valsalva) Projecting into the Conus Arteriosus Directly below the Junction of the Posterior and Left Anterior Pulmonary Cusps; and (*b*) the Communication lying also in the Conus directly subjacent of the Septal Defect with the Left Ventricle; (*c*) Vegetative and Ulcerative Endocarditis of the Pulmonary Valves and of the Mural Endocardium Adjacent and Opposite to the Ruptured Aneurysm; (*d*) Dilatation of the Pulmonary Artery.

From a drawing by Dr. J. H. Atkinson.

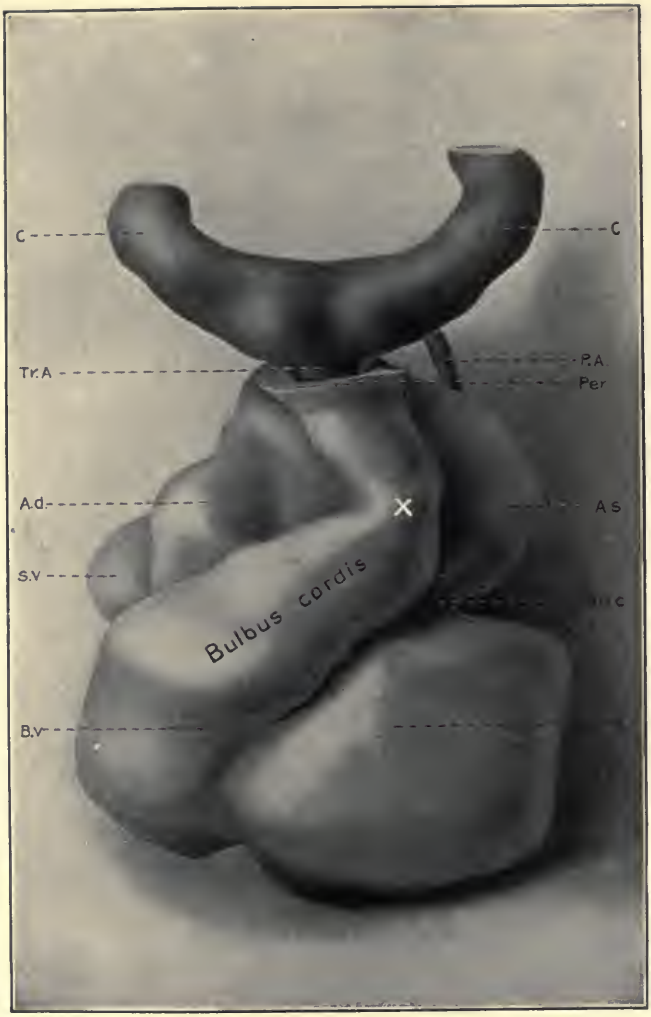

FIG. 3. MODEL OF THE HEART OF A HUMAN EMBRYO 4.6 MM. LONG X 108, TO SHOW THE RELATION OF EMBRYONIC BULBUS CORDIS TO VENTRICLE AND AORTIC ARCHES.

(The Division of the Bulbus Cordis into Aorta and Pulmonary Artery begins a little above the level of the Bulbo-Ventricular Cleft (B.v.), and from this point to the level of the Aortic Semilunar Cusps the "Bulbar" Septum Forms the Anterior Part of the Interventricular Septum of the Heart.) *C.*, Carotid Arch; *P. A.*, Pulmonary Artery; *Per.*, Pericardium; *Tr. A.*, Truncus Arteriosus; *A. d.*, Right Auricle; *A. s.*, Left Auricle; *Au. c.*, Common Auriculoventricular Orifice; *B. v.*, Bulboventricular Cleft; *V.*, Common Ventricle. Model by F. T. Lewis and M. E. Abbott, (Dr. Begg's Embryo).

(*From the Anatomical Laboratory of the Harvard Medical School.*) *Republished from Osler and McCrae's "System of Medicine," 2nd Edition, 1915, p. 324.*

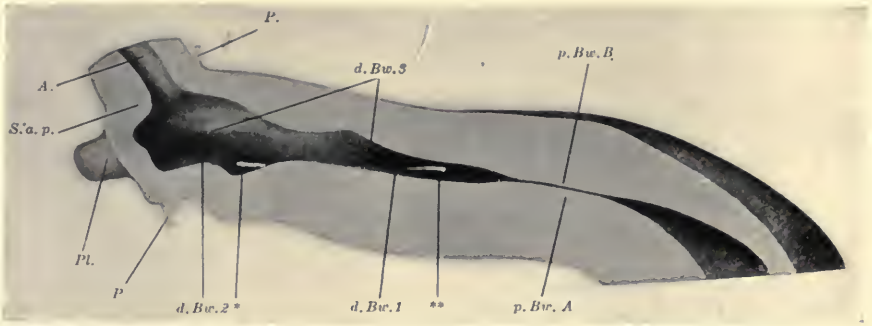

FIG. 4. LEFT HALF OF MODEL BY JULIUS TANDLER OF THE BULBUS CORDIS OF THE EMBRYO H_6, DIVIDED LONGITUDINALLY.

Showing Stage of Development in which the Distal Bulbar Swellings 1 and 3 (from which the Aortic and Pulmonary Cusps Originate) have Fused to Form the Distal Bulbar System, the Proximal Bulbar Swellings (*p. Bw. A.B.*) have Fused to Form the Proximal Bulbar Septum, and the Septum Aortico-pulmonale (*S.a.p.*) has Grown Downward for a Short Distance, Leaving two Points of Communication between the Aortic and Pulmonary Trunks, Immediately above and below the Distal Bulbar Septum (Aortic and Pulmonary Cusps). The Sound in the Picture has Disappeared in the Lumen of the Pulmonary Artery and Reappears in the Common Lumen above and below the Distal Septum at these Two Points of Communication. These Points thus Correspond in Location to the Openings above and below the Right Aortic Cusp Seen in Case Reported.

"*A.*, Aorta (4th Aortic Arch); *D. Bw*, 1–3, Distal Bulbar Swellings; *P.* Attachment of Pericardium; *p. Bw. A. B.*, Proximal Bulbar Swellings *A.B.*; *Pl.*, Pulmonary Artery (Sixth Aortic Arch); *S.a.p.*, Septum Aorto-pulmonale;*, point at which the sound of the Lumen of the Pulmonary Artery disappears, being covered by the Fusion of the Distal Bulbar Swellings 1 and 3, forming the Distal Bulbar Septum;** point at which the sound again appears in the Common Lumen. The subdivision of the Common Efferent Tube is produced distally by the Septum Aorto-pulmonale, in the middle region by the Distal Bulbar Septum, and Proximally by the Proximal Bulbar Septum. Between these three portions of the partition there are two points of communication, in which the ends of the sounds are visible."

From Keibel and Mall's "Embryology," Vol. II, Fig. 384, p. 552.

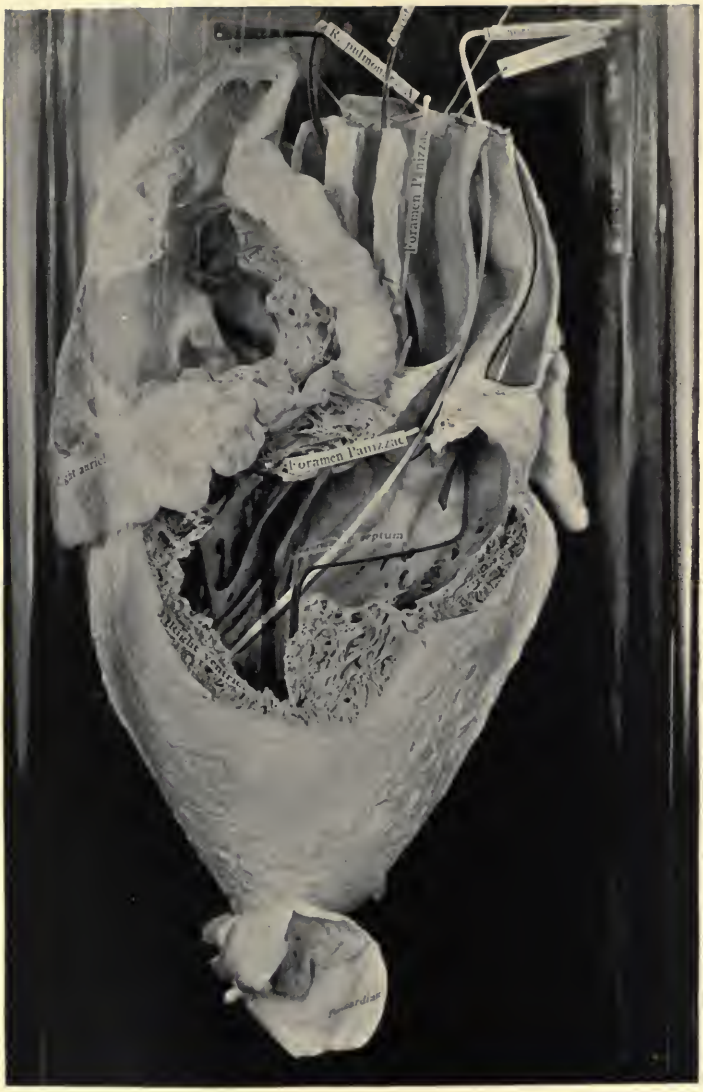

FIG. 5. HEART OF ALLIGATOR MISSISSIPPIENSIS.

View Showing Right Chambers, Pulmonary Artery and Left Aortic Arch (Arising Anteriorly from Right Ventricle), also Right Aortic Arch (Arising Posteriorly from Left Ventricle).

The Foramen Panizzæ lies behind the Posterior Cusp of the Left Aorta (in right ventricle), and Communicates with the Right Aorta *just behind its Anterior or Right Coronary Cusp* (in left ventricle) (which is the Location of the "Aneurysm of the Right Aortic Sinuses of Valsalva"). It is marked by a white rod. The Right Aortic Arch is marked by a dark rod. It slants obliquely upward from left to right and gives off in its course the Carotid Arch.

From a specimen in Professor Huntington's Anatomical Museum, College of Physicians and Surgeons, Columbia University, New York.

and slight œdema developed, but never any cyanosis. The patient died March 5, 1915.

Clinical Diagnosis. Aortic insufficiency. Congenital or acquired communication (probably ruptured aneurysmal) between aorta and pulmonary artery or base of right ventricle. Malignant endocarditis, or endarteritis, about the margins of the communication.

The autopsy was done by Professor Horst Oertel, from whose report the following abstract is quoted, with his kind permission.

Body, 180 cm. long, of indifferent physique and poor nutrition. Skin pale, petechial hæmorrhages on thighs, œdema of legs. Chest bulging.

On opening thorax precordial area occupied largest part, goodly amount of clear yellow fluid in both pleural and peritoneal cavities. Pericardium contains 200 c.c. clear fluid, parietal pericardium free, thin, no pleuropericardial adhesions. Aortic and pulmonary valves the seat of an extensive productive ulcerative endocarditis which leads to the formation of massive polypoid vegetations and loss of substance on the cusps of the valves and on the right side on the parietal endocardium adjoining the valve. Two perforations exist, leading to communications between left and right sides of heart. The first takes its origin from the sinus of Valsalva of the middle aortic cusp, and forming an aneurysmal pouch or trumpet which projects into the right ventricle between the septal and middle cusps of the pulmonary, has perforated into the right heart. The second perforation exists immediately below this, and extends through the septum of the ventricles by an irregular ulceration of the musculature, immediately below septal cusp of the aorta to immediately below septal cusp of the pulmonary artery. A few small verrucose vegetations on mitral. Tricuspid quite free, also auricles. Marked hypertrophy of both sides of heart.

Lungs compressed, œdematous, and contain multiple hæmorrhagic infarcts. Congestion of ileum and œdema and congestion of large intestine. Cyanosis of liver. Spleen weighed 375 grams, enlarged, firm, dark red. Hæmorrhagic and productive nephritis.

A detailed description of the heart, which was handed over to the writer for further study, follows:

A heart greatly dilated and hypertrophied in its left ventricle and auricle, and also, though to a less extent, in its right chambers. Depth of left ventricle from base of anterior aortic cusps to apex 12 cm., thickness of wall 1.6 cm., thickness of right ventricle 6 cm. Pulmonary artery and orifice dilated, circumefrence at valves 8.5 cm. Circumference of aorta at same level 6.5 cm. Aortic and pulmonary cusps thickened and insufficient, and covered with recent vegetations which extend upon the

upper surfaces of the aortic cusps and upon the mural endocardium of the base of both ventricles, and are especially redundant in the conus of the right ventricle on its anterior and septal walls.

The right anterior[3] aortic sinus of Valsalva presents in its floor, below the orifice of the right coronary artery, a large orifice admitting the finger, which leads into a tubular trumpet-shaped process, 2 cm. long, which projects into the right ventricle between the septal and median pulmonary cusps, and represents a ruptured aneurysm of the sinus. The walls of this tubular canal are thick and tendinous, and are covered externally in the conus of the right ventricle by polypoid vegetations, and the free borders of its ruptured orifice are fringed with vegetations which have impinged upon the opposite (anterior) conus wall and have evidently led by secondary infection to the development of a great patch of vegetations 5 cm. square, which occupies this position. (See Plate II.)

Directly below the right anterior cusp in the left ventricle is seen a second opening leading into the conus of the right ventricle. It is of ovoid shape, about 1 cm. long, and has as its upper border the base and ventricular surface of the right aortic cusp, which on its aortic surface is continuous with and helps to form the floor of the trumpet-shaped aneurysm of the sinus. The lower and anterior borders of this interventricular opening on the side of the left ventricle are rounded and muscular, but this is partly obscured by tendinous thickening and by a superimposed flattened film of vegetations. (See Plate I.) The posterior border of the defect lies 1.5 cm. anterior to the pars membranacea, that is, it is not in the situation usually occupied by interventricular septal defects, but lies in the extreme anterior or bulbar part of the interventricular septum in the usual situation occupied by bulbar septal defects. Seen from the right ventricle this interventricular communication opens into the conus immediately below and to the left of the ruptured sinus aneurysm. Its edges are ulcerated and destroyed, and it is surrounded by masses of vegetations.

The left anterior aortic cusp is displaced downward 5 cm. below the left coronary, and an interval of 1 cm. exists between it and the right anterior cusp. This interval is filled with a mass of vegetations, and these have burrowed freely into the myocardium adjacent.

Remarks upon this Case. *Clinical.* 1. As has been said, the diagnosis of a communication between the base of the aorta and

[3] A note upon the nomenclature of the aortic cusps is necessary. Gray, Morris, mention an anterior (right coronary) and two right and left posterior (left coronary) cusps. But that used by the older writers and in the German articles is right and left anterior (right and left coronary) and posterior (free) cusp, and it is this terminology that is followed here.

the pulmonary circulation, which was so obvious here, was based on the localization of maximum intensity of the continuous murmur and thrill over the middle of the precordium, and the intensity and extraordinary proximity of these signs to the chest wall, which differentiated it from patent ductus. The question as to the time the communication occurred, that is, whether it had been present throughout life (indicating a congenital perforation) or had existed for some years (pointing to a ruptured aneurysm), or was synchronous only with the present attack of malignant endocarditis, and due possibly to its ravages, was of equally great interest. In view of the intelligence of the patient, his emphatic assurance that the precordial vibration, which was perfectly evident to his sight and touch, had appeared at the time of his first cardiac breakdown, nine years ago, and had persisted since, was important. Since, however, the diagnosis of an aneurysm rupturing at this time depended on the accuracy of this statement, it was important to confirm it. Through the kindness of Professor Arthur Keith, London, the following facts were obtained from the Grantham Hospital, England. The patient was sent in by Dr. G. M. Shipman, and the entry relating to him in the hospital case-book read: "G. R., aged twenty-seven, admitted August 14, 1905. Discharged May 3, 1906. Disease, aneurysm of the aorta. Result, in statu quo." Dr. Shipman further wrote Dr. Keith "Re G. R.," that he "remembered the case of aneurysm of the aorta perfectly, and would look up some notes which he had about him." Owing to the war exigencies these notes have not yet been received, but the above information is sufficiently confirmatory of the patient's statements to make the diagnosis of aneurysm of the base of the aorta rupturing into the pulmonary circulation nine years before death a practical certainty.

2. The marked *diastolic* character of the almost continuous murmur was of interest. This was present also in several of the cases, but is not a constant feature, and may have had to do with the rough vegetations at the orifice of the trumpet-shaped tube through which the blood passed in diastole. The complexity of the other murmurs present is readily explained by the aortic and pulmonary insufficiency that existed, and the masses of vegetations that blocked the pulmonary conus.

3. The marked dyspnœa, without cyanosis, was confirmatory

evidence that the course of the blood through the ruptured aneurysm and ventricular communication was from the left to the right heart, owing to the fact that the pressure is physiologically highest in the left (systemic) ventricle. In such cases the volume of blood in the pulmonary circulation is necessarily increased. An effort was made to obtain confirmation of this by determining the basal carrying tension of the alveolar air for oxygen according to the method suggested by Plesch, (16) but no results were obtained owing to inadequacy of apparatus.

4. The youth of the patient at the first onset of symptoms, together with the complete absence of luetic history, suggested a traumatic or congenital origin of the ruptured aneurysm. He gave a history of striking his chest violently over the precordium against a pointed instrument (semaphore) at the age of four, and this trauma was insisted upon as a cause by himself and by his father, who wrote us several letters. The idea was discarded by me as improbable, in favour of a probably congenital origin with rupture as a result of strain.

5. The septic temperature and chills, which grew progressively worse, pointed definitely to an acute infective process which was believed by me to be secondary to the ruptured aneurysm.

Pathological Anatomy. The pathological interest of this specimen lies in: (1) the ruptured aneurysm of the right aortic sinus of Valsalva; (2) the interventricular communication directly below the same aortic cusp; (3) the marked thickening of aortic and pulmonary valves and evidences in the great size and thickness of the left ventricle of an aortic insufficiency of long standing; (4) the extravagant vegetations of malignant endocarditis, which cover the aortic and pulmonary cusps, surround the margins of the interventricular communication, especially in the right ventricle, fringe the borders of the ruptured aneurysm, and cover the opposite wall of the right ventricle.

The presence of such an extensive acute infective endocarditis, together with the evidences of an old inflammatory process, obscures the nature of the two openings into the right ventricle somewhat, and led to a difference of opinion at the autopsy as to their nature—their irregular ulcerated outline, especially on the side of the right ventricle, and their encrustment with vegetations suggesting a

possible inflammatory origin. The clinical history of the case, however, pointing to a ruptured aneurysm of nine years' standing; the finger-like character and position of this aneursym, identical in all respects with the cases reported, in which an exactly similar tube with thin membranous walls and without any sign of inflammation projected into the right ventricle in an exactly similar situation; the location of the ventricular communication directly below the same aortic cusp and having this cusp as its upper border; its situation in the anterior upper part of the ventricular septum and opening into the conus of the right ventricle in the typical situation for bulbar septal defects (cases reported by Tate, (17) Coupland, (18) Rolleston (19)); its shape and character as seen from the left ventricle, where the ravages of the malignant endocarditis are less serious; above all, the combination of these two conditions, namely, aneurysm immediately above and ventricular communication immediately below the right aortic valve, as occurred in the other cases recorded in which there was no sign of inflammation and in which a congenital origin was concluded, led the writer to conclude that both openings are here of congenital origin, due to a thinning above and a defect below of the bulbar septum between the two great trunks which, in the submergence of the embryonic bulbus cordis, forms the extreme upper and anterior part of the interventricular septum, the congenitally thin wall of the right aortic sinus yielding under the pressure of the circulation and forming the trumpet-shaped pouch which projected into the right ventricle and ruptured as a result of strain. The great redundancy of the vegetations in the pulmonary conus supports the view of their secondary origin about the defects, for it is not usual for endocarditis to develop in this situation without determining cause.

Development. A study of the development of the aortic and anterior part of the interventricular septum gives striking confirmation to the view that both sinus aneurysm and septal communication are due to a defective development of the embryonic bulbar septum. As is well known, in the earlier stages of the embryonic heart, the arterial trunk or efferent tube consists of the muscular bulbus cordis of the ventricle, which gives off the embryonic aortic arches from its upper border (see Plate III), and is lined by endocardial swellings spirally arranged (which persist in some of the

fishes as rows of valves). As division of the heart proceeds by development of its septa the division of the primitive arterial trunk takes place in the part derived from the bulbus cordis by fusion of the "proximal" and "distal" pairs of bulbar swellings, and at the extreme distal end by a septum growing down from above between the aorta and the pulmonary artery. The distal bulbar swellings correspond to the site of the future aortic cusps. There thus exists a stage in the development of the aortic septum in which the septum aortico-pulmonale is growing downward from above, the distal bulbar swellings have united in the middle and the proximal bulbar swellings are united below, leaving two apertures where the arterial trunk is still common immediately below and above the future aortic and pulmonary cusps. This stage of development has been reconstructed by Julius Tandler and is figured in Keibel and Mall's "Embryology," 2d edition, Fig. 384, and the plate is reproduced in this article. The probe passes from the lumen of the pulmonary artery through two apertures which occupy the exact location of the defects seen in the cases of aneurysm of the right aortic sinus of Valsalva and the anterior interventricular septal defects in the cases described by Hale-White, Thurnam, Kraus, Hart, and in the specimen which forms the subject of this paper.

Comparative Anatomy. A study of the hearts of reptiles and amphibians, made for confirmatory purposes in Professor Huntington's Collection at Columbia University, New York, elicited the extremely interesting information that this aperture above the anterior aortic cusp of the right aorta in the crocodile remains permanently open and allows the aerated blood from the right aortic arch (which arises from the left ventricle and supplies the systemic circulation), to pass into the left aortic arch (which arises from the right ventricle and receives unaerated blood) through an aperture above its posterior cusp. This is the so-called foramen Panizzæ of the crocodile (see Plate V), and the aneurysm of the right aortic sinus would seem to represent a persistence of the same opening. It was seen in the human subject not as an aneurysm, but as a complete defect in the cases reported by Rickards and Charteris. This view is confirmed by a perusal of the comprehensive studies by Langer (22) and Greil (23) upon the developmental changes in

the reptilian bulbus cordis in successive stages, which gives interesting confirmation, from the field of comparative embryology, of Tandler's reconstruction.

Summary of Literature. For purposes of comparison the cases in the literature of congenital communications, or aneurysm, of the right aortic sinus of Valsalva into the right ventricle, are herewith briefly summarized.

I. Thurnam (7) (1840). "Ruptured Aneurysm of Right Aortic Sinus of Valsalva. Malignant Endocarditis." Aneurysm projecting into and communicating by two rounded openings with base of right ventricle; recent endocarditis; pulmonary, aortic, and mitral insufficiency; hypertrophy and dilatation of heart.

Male, aged thirty-three. Rheumatism at twenty. Sudden onset while in perfect health, with sense of "cracking" in heart region, of faintness, palpitation, dyspnœa, hæmoptysis, anasarca, extraordinarily superficial continuous sawing murmur with tremor intense in left second interspace. Death eleven weeks later.

II. Beck (2) (1842). "Ruptured Aneurysm with Interventricular Communication." Right aortic valve calcified, sinus enlarged, presenting round opening leading into collapsed sac-like glove-finger three-quarters inch long, projecting into right ventricle between healthy pulmonary valves. Three rounded openings in tip and sides. Below it, interventricular communication admitting goose-quill, believed by author to be congenital.

Male, aged thirty-one. Palpitation on exertion always. Signs of cardiac insufficiency and marked dyspnœa three years, anasarca developed. Very superficial sawing murmur with tremor, loudest in diastole but continuous, with maximum intensity at base of heart.

III. Rickards (1) (1881). "Congenital Communication in Right Aortic Sinus with Right Ventricle. Septal defect." Right and left anterior aortic valves congenitally fused, behind right half large round orifice with smooth membranous funnel-shaped walls opening into right ventricle between healthy pulmonary cusps. Immediately below same cusp circular aperture in septum with smooth membranous walls passing into conus of right ventricle. Both openings considered by author congenital.

Male, aged thirty. Precordial discomfort and dyspnœa always. Loud, rough, double murmur practically continuous, systolic element loudest, maximum between third cartilages, intense purring double precordial vibration. Epistaxis, hæmoptysis.

IV. Charteris (15) (1883). "Congenital Communication in Right Aortic Sinus with Right Ventricle." Immediately behind right aortic valve rounded opening with firm margins leading into right ventricle. Patch of endocardial thickening on opposite wall of right ventricle.

Male, aged fifty-three. Died from cardiac insufficiency. Systolic murmur most distinct at apex.

V. Krzywicki (4) (1889). "Ruptured Aneurysm of Right Aortic Sinus." In sinus oval opening with tendinous borders leading into thimble-shaped cavity 2.5 cm. deep, extending into right ventricle with thin, almost transparent, membranous covering formed of very delicate connective tissue with endocardial covering derived from right ventricle. Bean-shaped perforation at apex.

Female, aged twenty. Nine months before death pleurisy, precordial pain, palpitation, anasarca. Systolic murmur over base.

VI. Hale-White (3) (1891). "Ruptured Aneurysm of Right Aortic Sinus with Septal Defect." Septum deficient just below right aortic valve, ovoid opening margins thickened, septum for three-quarters inch around thin, semitransparent. Sinus above valve, thin-walled pouch which bulged three-quarters inch into right ventricle with aperture at bottom. Two patches of endocardial thickening on wall of right ventricle opposite defects.

Male, aged fifteen. Symptoms four months, dyspnœa, œdema, precordial vibration, rasping to-and-fro murmurs simulating pericardial friction, maximum at third interspace.

VII. Kraus (5) (1902). "Ruptured Aneurysm of Right Aortic Sinus. Interventricular Communication. Old Endocarditis." Wall of right aortic sinus thinned and membranous, pushed into right ventricle just below pulmonary valves as sac 2.5 cm. long, carrying on anterior surface diverticulum with delicate walls, perforated at apex. Walls of sac smooth and glistening. Semilunar opening in septum just below right aortic cusp. Endocardium surrounding this extensively scarred.

Male, aged twenty-seven. Symptoms four years, onset after severe muscular strain. Dyspnœa, palpitation, cyanosis, anasarca, hæmoptysis. Marked systolic thrill and coarse, long systolic murmur almost continuous, with short, hissing, roaring diastolic element, maximum at second and third interspaces.

VIII. Hart (6) (1905) (Case III). "Ruptured Aneurysm of Right Aortic Sinus. Septal Defect. Malignant Endocarditis." Semilunar opening in septum just below right aortic cusp, opening in conus of right ventricle. Just above it, sacculation, size of walnut, of right aortic sinus with extremely transparent membranous wall reaching forward

into pulmonary conus in semicircular form just between right pulmonary cusps. Fibrous ring below aortic valves. Malignant endocarditis of margins of septal defect, left pulmonary cusp, and fibrous ring, considered by author secondary to septal defect and sinus aneurysm of congenital origin.

IX. Author's Case (1919). "Ruptured Aneurysm of Right Aortic Sinus. Interventricular Communication (believed to be Bulbar Septal Defect). Malignant Endocarditis."

Male, aged thirty-six. Onset of symptoms nine years before death with dyspnœa, precordial vibration and sawing, continuous murmur with diastolic accentuation. Cardiac efficiency re-established after two years' illness, but physical signs persisted. Second cardiac breakdown with malignant endocarditis nine months before death.

Conclusions

1. A case is reported of aneurysm of the right aortic sinus of Valsalva rupturing into the right ventricle associated with interventricular communication and malignant endocarditis.

2. The presence of the characteristic physical signs of communication between the base of the aorta and the pulmonary circulation, namely, coarse precordial vibration and continuous sawing murmur with diastolic accentuation superficially placed, and with maximum intensity over the second and third interspaces, justified this diagnosis, which was made during life.

3. The clinical evidence accumulated was sufficient, in the judgment of the writer, to warrant the conclusion that the aneurysm ruptured into the right ventricle nine years before death. During this time the patient maintained a moderate degree of cardiac efficiency, showing that communication between the two circulations is compatible with life for a long time.

4. The aneurysm of the right aortic sinus and the interventricular communication are believed by the writer—on the ground of their location immediately above and below the right aortic cusp, the shape and appearance of the septal opening seen from the left ventricle, the evidence of identical cases in the literature unassociated with malignant endocarditis, and the facts of development and comparative anatomy,—to be of congenital origin, and due to defective development of the bulbar septum between the aortic and pulmo-

nary trunks which forms the upper anterior part of the ventricular septum in the submergence of the bulbus cordis.

5. There is a stage in the development of the aortic septum at which two such apertures exist above and below the "distal bulbar septum" which is the site of the aortic and pulmonary valves. The upper of these apertures remains permanently open in the crocodile as the foramen Panizzæ, which is thus the homologue of the aneurysmal thinning or congenital opening which occurs in the right aortic sinus of Valsalva.

6. The malignant endocarditis, which is so extensive in this case as to obscure the two openings in the side of the right ventricle, is believed by us to be secondary to the two defects. The extravagance of the vegetations in the conus of the right ventricle supports this assumption, for such processes rarely develop in this situation without a determining cause.

In conclusion, the writer's sincere thanks are due to Professor W. F. Hamilton for the privilege of studying this remarkable case during life, to Professor Horst Oertel for placing the heart at her disposal, to Dr. Arthur Keith for the valuable information obtained through his kindness from the Grantham Hospital, to Professor G. S. Huntington for the privilege of studying his admirable embryological and anatomical Museum Collections, and for his kindness in giving this case his consideration and confirming the explanation here given of the developmental origin of the two defects, and to Sir William Osler for inspiration and encouragement in the study of congenital hearts.

BIBLIOGRAPHY

1. Beck, "Aneurysm of Ascending Aorta Bursting into Right Ventricle with a Communication between the Two Ventricles," *Medico-Chir. Tr.*, 1842, XXV, 15.
2. Hale-White, "A Case of Patent Ventricular Septum, together with an Aneurysm of the Base of the Aorta Opening into the Right Ventricle," *Tr. Path. Soc.*, Lond., 1891–92, XLIII, 34.
3. Krzywicki, "Aneurysms of the Right Aortic Sinus of Valsalva," *Zieg. Bertr.*, 1889, VI, 473.
4. Kraus, "True Aneurysm of the Right Aortic Sinus of Valsalva," *Berl. klin. Wchnschr.*, 1902, XXIX, 1161.

5. Hart, "Aneurysm of the Right Sinus of Valsalva of the Aorta and its Relation to the Upper Ventricular Septum," *Virch. Arch. f. path. Anat.*, 1905, CLXXXII, 167.
6. Thurnam, "Aneurysms, and Especially Spontaneous Varicose Aneurysms of the Ascending Aorta, and Sinuses of Valsalva." Case VII. "Spontaneous Varicose Aneurysm of the Right Aortic Sinus and Summit of the Right Ventricle of the Heart," *Medico-Chir. Trans.*, 1840, XXIII, 337.
7. Peacock, "Aneurysm of the Ascending Aorta, Pressing upon the Base of the Right Ventricle and Opening into the Origin of the Pulmonary Artery; with Remarks on the Communication of the Sacs of Aneurysms with the Cardiac Cavities and Adjacent Vessels," *Tr. Path. Soc. Lond.*, 1868, XIX, 111.
8. Brocq, "Étude sur les Communications entre l'Aorte et l'Artère Pulmonaire autres que celles qui résultent de la persistance du Canal Artériel," *Rev. de méd.*, 1885, V, 1046, and 1886, VI, p. 786.
9. Rickards, "Six Cardiac and Vascular Cases. Case II. Communications between the Aorta and Pulmonary and between the Right and Left Ventricle; Two Aortic Segments," *Brit. M. J.*, 1881, II, 71.
10. Wilkes, "Communication between the Pulmonary Artery and Aorta," *Trans. Path. Soc., Lond.*, 1860, XI, 57.
11. Baginsky, "Communication between Aorta and Pulmonary Artery," *Berl. klin. Wchnschr.*, 1879, XLIII, 420.
12. Fräntzel, "A Case of Abnormal Communication of Aorta with Pulmonary Artery," *Virch. Arch.*, 1868, XLIII, 420.
13. Girard, "Case of Congenital Communication between Aorta and Pulmonary Artery," Zurich Thesis, 1895.
14. Hektoen, "Rare Congenital Anomalies. Case I. Large Defect in Septum between Pulmonary Artery and Aorta, the Heart normally Developed. General Infection with Bacillus Mucosus Capsulatus," *Tr. Path. Soc. Chicago*, November 12, 1900.
15. Charteris, "Notes on a Case of Congenital Malformation of the Heart, Opening between Aortic Valves and Right Ventricle, *Med. Press. & Cir.*, 1883, XXXV, 354.
16. Plesch, "Zur Diagnose der kongenitalen Vitien," *Berl. klin. Wchnschr.*, 1909, XLVI, 390.
17. Tate, "Case of Malformation of the Heart with Perforation of Ventricular Septum," *Tr. Path. Soc. Lond.*, 1892, XIII, 36.
18. Coupland, "Defect in the Ventricular Septum of the Heart, Probably Congenital; unusual Site of Aperture," *Tr. Path. Soc. Lond.*, 1879, XXX, 266.

19. Rolleston, "Communication between the Ventricles of the Heart," *Tr. Path. Soc. Lond.*, 1891, XLII, 65.
20. Roberts, "Aneurysm of Root of Aorta Communicating with Pulmonary Artery," *Brit. M. J.*, May 2, 1868, No. 383.
21. Gairdner, "Aneurysm of First Part of Artery Opening into Pulmonary Artery and Conus Arteriosus of Right Ventricle," *Glasg. Hosp. Rep.*, 1899, 1.
22. Langer, "On the Development of the Bulbus Cordis in Amphibia and Reptiles," *Morph. Jahrb.*, XXI, 1894.
23. Greil, "Contributions to the Anatomy and Development of the Heart and Truncus Arteriosus in Vertebrates," *Morph. Jahrb.*, XXXI, 1903.

DETECTION OF ABNORMAL TISSUES WITHIN THE LUNGS

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ONE of my most vivid memories of the teacher to whom this volume is dedicated is the way in which he introduced to the subject of physical diagnosis the group of medical students to which I belonged. He traced the early history of palpation, auscultation, and percussion, and pointed out the indifference with which these methods were first met, and then the difficulties which they long suffered, and which they too often still suffer from lack of careful, objective, discriminating study. He emphasized above all the need of co-ordinating study of physical diagnosis with that of normal and morbid anatomy.

Since my student days there has arisen an important addition to the time-honored methods of physical diagnosis, that of roentgenology. A great addition has thus been made, especially to methods of physical examination of the thoracic cavity. But, like the older methods, this new method is either too frequently treated with indifference or fails to receive the accurate objective study, coupled with studies of morbid and pathological anatomy and experimental work on animals, necessary for fruitful yield.

Thus, for instance, in the study of the heart, the roentgen rays offer us a far more accurate method of determining its size and some features of its activity than any we have hitherto had. Yet the majority of the relatively few who as yet make use of the roentgen rays in the clinical diagnosis of cardiac conditions do no more than measure the transverse diameter of the heart silhouette, and gain little more information than may be gained by expert percussion.

So, also, in the study of the lungs, very few have carefully correlated roentgenological study of the lungs with the study of normal and morbid anatomy, as H. K. Dunham has done in co-operation with W. S. Miller.

The extent of the possibility of distinguishing within the lungs

relatively minute tissue alterations is appreciated by few, even of the expert roentgenologists. Thus in the first edition of the rules for medical examination under the Selective Service Act the statement is made that "Tubercle caseations as such cast no shadows distinguishable from the other tissues of the parenchyma." That "it has been found that cubes 1 c.c. in size of caseous tubercle, when embedded in a healthy lung, are indistinguishable by the *x*-ray." Just how the experiment was conducted is not stated, but when I read this statement it struck me as improbable that it could be true. I, therefore, devised the experiments described below and had them carried out by two of my student assistants, Mr. H. K. Kasten and Mr. Louis Hanson, who embodied their work in a thesis for the B. S. degree. This thesis, illustrated by numerous photographs, is now deposited in the library at the University of Wisconsin. Valuable aid in the work was contributed by Dr. Howard Curl, roentgenologist at the University of Wisconsin.

For the work large dogs were selected, several of them with an anteroposterior chest diameter larger than that of the average man. The dogs were killed, one or more small openings were made in the intercostal spaces at the side, opposite the lines of separation between the lobes of the lung, small pieces of tissues were inserted between two lobes, and the lungs were inflated. Pieces of tissue were thus embedded in the midst of lung tissue without injury to the lungs. The lungs, after inflation, were studied fluoroscopically and then stereoscopic pictures were taken. In some cases small pieces of metal were inserted as markers. In other cases, in order to eliminate the possibility of the action of secondary rays, no such markers were used. The experiment was varied by tying the urinary bladder of a small rabbit on the end of a small glass and inserting this between two of the lobes. It was then possible to introduce water or other fluids into this bladder and determine the quantity necessary to make the bladder visible fluoroscopically or in the roentgenogram.

The most surprising result of these experiments was that minute pieces of tissue, which when embedded in the skin or muscles of the body wall are invisible, stand out clearly when in the lung tissue, although they should obstruct the passage of the rays as little in the one case as the other. This was true even with the fluoroscope, and was strikingly so with stereoscopic photographs.

As a routine, blocks of fresh animal tissue were cut as nearly cubical as possible. Some spherical pieces were also used. The pieces varied in size from a diameter of ½ to that of 1 cm. Of the tissues studied cartilage was the most opaque. A piece a few millimeters in diameter could be distinguished within the lung even in animals in which the cartilaginous ribs could not be distinguished roentgenologically. The relative opacity of cartilage is important to bear in mind, since the bronchial cartilages, especially when perpendicular to the rays, may lead one to think of tubercles. Of the other tissues tried, liver, kidney, spleen, and muscle tissue seemed to be about equally opaque to the rays. In the rabbit-bladder experiment in a large dog about .5 c.c. of water was sufficient to give a visible shadow.

From these experiments we may, therefore, conclude that it is possible to distinguish by means of the roentgen rays much more minute alteration in the tissues than many observers have as yet been willing to acknowledge, and that the limits of diagnosis of pulmonary lesion by means of the roentgen rays are far from reached. What is needed is a careful correlation between roentgenology and normal and pathological anatomy.

THE CONDITIONS PRESENTED IN THE HEART AND KIDNEYS OF OLD PEOPLE

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OLD age is to be regarded as a part of the evolution of the body; it is not a pathological condition produced by the agency of causes external to the organism, but the source of the essential changes in the tissues which constitute the condition is inherent in the germ. The phenomena which are exhibited by the aged individual, differing as they do from the phenomena of earlier life, are due to changes which have gradually taken place in the material of the body. It is impossible to comprehend age without recognizing that we have to do with a body differently constituted from that of earlier life. Some of the changes have begun early, others are late in appearance, some are easily recognized, and certain of the changes, non-recognizable by present methods, must be assumed from the differences in the reaction of the material. The mode of development, the character of these changes, and the reactions of the body so altered constitute the anatomy and physiology of old age, about which we know very much less than we know of the body and its reactions in any other period of life. There is a further complexity in the condition, in that the diseases of earlier life have produced changes which may accelerate or certainly complicate the development of those changes which are to be regarded as physiological. In the pathology of age we have to do with lesions which are imposed upon the aged organism by external causes. Death in the period may come as the result of disease, just as at any other period of life, but there is also what may be regarded as physiological death, due to the advancing changes becoming so great that function is impossible. There is great individual difference in the period of development and in the rapidity of advance of the changes of age, but they always appear.

Anyone studying the subject of old age becomes aware of the lack of knowledge of the condition when he seeks in literature

answers to the questions which constantly present themselves, and this is even more striking in the study of old age in animals. There is no mammal whose life history, comprising anatomy and physiology, we know from beginning to end, and in all cases we know more about the first period of life than the last. We do not know the basic metabolism of age nor whether this differs from the metabolism of other periods. It is true that old men, impatient of the lack of consideration and interest given to their condition, have written of the philosophy and even the diseases of age, and though some have written delightfully, they have given little information. There is little interest in the condition on the part of the men who have both the ability and the opportunities for investigation. Old people form but little part of the population of our best hospitals, and the chief interest in the last thirty years has been rather in those diseases and conditions to which the old are relatively immune.

I shall present in this paper the results of the study of the heart and kidneys in the autopsies of 580 individuals of the age of sixty and above. Of these cases 489 were taken from the records of the Pathological Department of the Harvard Medical School, and to these were added 92 cases taken from Wideroe's work on heart weights. The records from the school embrace 48 private autopsies, 197 from the Boston City Hospital, 148 from Long Island Hospital, and 95 from the Peter Bent Brigham Hospital. All these groups of cases show certain differences regarding age at death, weights of organs, etc., but these are all within the variations of chance, and a greater number of cases would probably have smoothed out these discrepancies. There is always difficulty in having routine pathological examinations accurately carried out, particularly when the stimulus which comes from close correlation between clinical and pathological interest is lacking, as it was in many of these old people. In most cases the histological slides of the autopsy material were examined, and as the result of this a few changes were made in the anatomical diagnoses. In the cases taken from Wideroe only the ages and weights of organs were accessible.

The age of sixty plus has been chosen for the study, because at this period changes are always present, and they become more accentuated as age advances. The average age of all cases is sixty-nine.[1] There is some difference in the average age of the different groups, the Boston City Hospital and Peter Bent Brigham Hospital giving sixty-six, the private

[1] In the figures the whole numbers to which the decimals most closely approximate are given.

autopsies sixty-nine, and the Long Island cases seventy-two. The expectation of life at the age of sixty in Massachusetts is 13.4 for males, and 14.8 for females, and this is closely approached by the Long Island cases. This institution takes care of a large number of aged poor, and has sent to it cases of chronic disease from the various hospitals. Wideroe's cases from Denmark have an average age of seventy-four, and his material was probably rather institutional than hospital.

The cases by age fall into the following groups: Sixty to sixty-nine, 347 cases; seventy to seventy-nine, 162 cases; eighty to eighty-nine, 59 cases; ninety, 12 cases.

The Heart. Hypertrophy is the most common pathological condition of the heart at these ages, and a primary division has been made dependent upon hypertrophy. The heart was removed by cutting the vessels just inside the pericardium; it was opened, all clots removed, and weighed with the epicardial fat. The amount of epicardial fat varies, but it is rarely sufficient in amount to place a smaller heart by weight in the class of hypertrophy. In determining hypertrophy, 350 grams has been selected as the limit of normal weight in the female, and 400 grams in the male. The weight of the normal heart has been the subject of many investigations, the most extensive being that of Müller, in which all epicardial fat was removed, the different parts of the heart—auricles, ventricles, and septum —weighed separately, and these weights compared with each other and the body weight. It is impossible to establish an index of heart weight in relation to body weight, owing to the variance in body weight, due to fat. The heart weight is influenced by the muscular development of the body, and the fat has very little influence. All records of weights of the normal heart, with the exception of those of Müller, agree that there is a gradual increase of weight up to the age of seventy, from which there is a slight decline. Beneke, who has made volume instead of weight determinations, shows that the volume follows the same law. Thoma gives an average weight:

Age	Average, Male and Female
60 to 70	332
70 to 80	321
80 to 90	303

Müller's weights, taken after removal of fat, are very irregular.

Age	Male	Female
40 to 50	288.8	239.8
50 to 60	277.6	229.9
60 to 70	257.9	262.6

His highest weight of the male heart is between the ages of forty and fifty, and of the female between sixty and seventy, in which he differs from all other authors. In Doctor Wolbach's autopsies of 26 young soldiers, ages twenty-one to thirty-one, who died of influenza at Camp Devens, an average of 335 grams was found, with variations between 245 and 425. That 350 grams in the female and 400 grams in the male are outside of the normal or usual variations is shown by the small number of weights close beneath these. The weights do not gradually increase to the hypertrophic weight, but by a sharp ascent. In the females there were 21 cases between 320 and 350 grams, and in the males 26 between 360 and 400 grams.

There were 248 hypertrophied hearts, or 42.77 per cent, and 332 non-hypertrophic. The weights of the non-hypertrophied hearts are by age:

	Males		Females		Male and Female
Age	Cases	Weights	Cases	Weights	Average
60 to 69	110	314	88	282	300
70 to 79	47	315	45	283	299
80 to 89	14	319	19	267	289
90+	5	321	4	294	309

The hypertrophied hearts gave the following:

	Males		Females		Male and Female
Age	Cases	Weights	Cases	Weights	Average
60 to 69	90	544	59	514	531
70 to 79	40	491	30	448	473
80 to 89	15	481	11	440	464
90+	3	455			455

There is but little difference in the relative numbers of hypertrophied hearts in the different groups. Wideroe's cases give 38 per cent, the Peter Bent Brigham Hospital 44 per cent, the private autopsies 33 per cent, the Long Island Hospital 41 per cent, and the Boston City Hospital 50 per cent. I can assign no reason for this high percentage of the City Hospital, unless it be that the cases going to this hospital represent more the working class of the population. The lowest is in the private autopsies, in which there is but small representation of this class.

One of the most common conditions found in the hearts of old people is valvular sclerosis. It affects both aortic and mitral valves, is rather more frequent in the former, and is very rare in the right heart. It consists in foci of necrosis with fatty and calcareous infiltration of the valve, and affects chiefly the ventricular aspect of the mitral valve and the concave

or aortic surface of the aortic valves. The aortic segment of the mitral is most frequently affected, but there is no preference in the aortic segments. In the mitral it is often associated with thickening of the free edge of the valve, and in 3 cases there was calcification of the ring of insertion. It is focal, and in the aortic valves begins with thickening and calcification of the line of insertion from which there is extension on the valves, both continuously and in small foci. The affected areas are opaque, stiffer than the normal valve tissue, and when calcified, hard and brittle. The adjoining edges of the aortic cusps may become adherent, and such masses of lime salts may be deposited as to produce stenosis. It is difficult to differentiate between this purely degenerative condition and that resulting from a healed valvular endocarditis. I have regarded as healed endocarditis those cases in which the condition was associated with thickening and shortening of the chordæ tendineæ of the mitral and irregular thickening and retraction of the aortic valves. The condition is not to be confounded with the extension of a syphilitic aortitis to the aortic valves. There were but 2 cases of this, and in general evidence of syphilis is rare at these ages. Such valvular sclerosis was found in 77 cases, 42 of these with heart hypertrophy, 35 without. In 16 of the cases it was extensive enough to produce stenosis of the aortic orifice, and in all of these there was hypertrophy. In 42 cases of chronic endocarditis there was hypertrophy in 25 cases. In 5 of the cases there was sufficient thickening and retraction of the mitral as obviously to interfere with function, and in 3 of these the heart was hypertrophied. There were 16 cases of acute endocarditis, 2 of these ulcerative and 3 verrucous, the others were terminal and consisted of thrombi, usually minute, on the edges of the valves in association with infection elsewhere.

The Myocardium. I have not considered the many cases of fatty degeneration. It is a pathological condition, and certainly in its highest degree indicates injury of the fibers most affected, but there is no clear evidence that it produces permanent injury, nor does it seem to interfere with function. It was as common in the hypertrophied as in the non-hypertrophied cases, and in general its frequency depends upon the care with which it is sought. There was 1 case of acute myocarditis with miliary abscesses, due to staphylococcus. Fibrous myocarditis was diagnosed in 86 cases, of which 60 were in the hypertrophied hearts, and varied in degree from small foci to large areas in which the entire thickness of the wall was substituted by fibrous tissue. In 3 of these there was globular dilatation of the heart at the affected area, constituting heart aneurysm. Some of the foci were recent, and necrotic fibers were found invaded by leucocytes, and in nearly all cases the adjoining muscle fibers were atrophic with diminution of fibrillæ. Generally in the hypertrophied hearts the fibers were large,

and the fibrillæ seemed not reduced in number. In 3 cases of hypertrophy fibers were found which showed an unduly large amount of sarcoplasm with reduction of fibrillæ, the condition described by Albrecht. In these cases there was much fibrous myocarditis, though not immediately associated with the affected fibers.

It was not possible to refer the fibrous myocarditis to circulatory disturbance due to arteriosclerosis of the coronary arteries. Where the foci were large, particularly those at the apex of the left ventricle, occlusion of the branch of the coronary which supplied the area was usually found. It was found associated with extensive disease of the coronaries, but also when the arteries were but slightly affected and extensive coronary sclerosis may coincide with a normal myocardium. There seems no doubt that fibrous myocarditis is very frequently due to degeneration of the muscle from lack of blood supply, and slowly advances, but much of it is the final result of myocardial injury associated with inefction. Infarction of the heart was found in 13 cases, and in 7 of these there was rupture. In all of these cases the wall of the left ventricle was affected, and either thrombosis or complete sclerotic closure of the corresponding coronary artery was found. Eight of the cases were in hypertrophied hearts.

In 8 cases the heart weighed less than 200 grams, and all these were in the decade from sixty to sixty-nine, the smallest, 125 grams, was in a small emaciated woman who had long been bedridden, and in none was there marked disparity between the size of the heart and that of the body. There were several cases of tumor metastasis in the heart, and 1 case in which it was displaced by the advance of a carcinoma of the lung. In some cases of general edema there was also edema of the myocardium with vacuolization of the fibers.

There were 46 cases of pericarditis, 29 of which were in the hypertrophied class, and 14 of the cases were acute. There were also 8 cases of hydropericardium due to circulatory disturbance, 7 of which were in the hypertrophied class.

In spite of the many pathological conditions which can be named, on the whole the heart in old people is a very good organ, and anatomically has suffered less from injury and wear than any of the large internal organs.

The Kidneys. The normal kidney varies considerably in weight, and the estimates of weight also vary. Thoma gives 306 grams as the average. Of his cases 50 were between 269 and 306, and 50 between 306 and 343. Wideroe's cases, at ages from twenty-five to fifty years, give for males 319 and females 306, an average of 313. Orth gives 320 for males and 293 for females. Wolbach has found in 26 autopsies on young soldiers, ages

twenty-one to thirty-one, who died of influenza, an average weight of 356, with variations from 150 to 460 grams. There were, however, pathological conditions which caused some increase in weight. The average weight in the cases considered here is 269 grams. This diminution in weight does not fairly represent the degree of atrophy. Cysts of the cortex are common and numerous; there is often considerable formation of fat in the pelvis following atrophy, often more or less thickening and adhesion of the capsule, and the weights of the large kidneys showing pyelonephrosis are included in the average weight. There is considerable decline in weight as age advances, with the exception of extreme age, when the weight of the kidneys, like that of the heart, increases. There is also considerable difference in the weights of the cases with hypertrophied hearts.

	Heart Hypertrophy		Non-Heart Hypertrophy	
Age	Cases	Weights	Cases	Weights
60 to 69	143	317	191	264
70 to 79	68	275	89	233
80 to 89	25	229	32	221
90+	3	265	9	233
Total cases	239		321	
Average weight		295		250

It is probable that some of the difference in weight of the hypertrophic cases is due to the more general prevalence of passive congestion in these.

There are few conditions which so generally repeat themselves as does that of the kidneys in old age. The capsule is usually slightly thickened and adherent, the surface beneath rarely smooth, usually finely granular, but the granulation is not so marked as in the genuine small granular kidney. There may be definite losses of substance due to old infarctions or other focal pathological conditions, but the coarse and irregular depressions generally regarded as characteristic of the arteriosclerotic kidney are not frequently found. On section the markings are not so evident as in the normal, both cortex and pyramids are reduced, the tissue is more lax, but tougher than normal, and cannot be broken on bending. Microscopically there are areas of atrophy and destruction involving both tubules and glomeruli, which are usually focal and close beneath the capsule. They are small, triangular, with a broad base on the surface, and they rarely extend through the cortex. The epithelium of the cortical tubules is low, is less granular than normal, the tubules appear dilated, the nuclei are small, contain less chromatin, and are fewer in number in the syncitium. In other parts of the cortex there are single destroyed glomeruli and some small areas of atrophic tubules. Measurements of glomeruli show diminution in size, and single groups of vessels in a glomerulus

become obsolete. The pyramids are smaller, the striation lost, and microscopically the interstitial tissue has lost its fibrillation, is hyaline, but still gives the collagen stain. There is often extensive destruction of the pyramidal tubules, forcing the conclusion that in some way new arrangements of tubules must have taken place. In every kidney examined casts were found in the tubules, usually in the Henle or small collecting tubules at the base of the pyramids, sometimes numerous, at other times few. This condition of the kidney I have designated *chronic atrophic nephropathy*, and it is as characteristic of age as is the shrunken shank and tottering gait. After studying these cases, to take up the sections which Dr. Wolbach has made from the kidneys of young soldiers gives the impression of passing from age to youth. I have found this condition, which in the protocols was variously described as chronic interstitial nephritis, senile nephritis, arteriosclerotic nephritis, vascular nephritis, etc., in 246 cases, 124 of these with hypertrophied hearts. Of the other forms of hematogenous nephropathy there was 1 of acute glomerular nephropathy and 6 of subacute and chronic—all of these in the heart hypertrophy class, and 7 cases of small granular contracted kidney, 2 of which were in the non-heart hypertrophy series. The total, 13, occurred in the decade sixty to sixty-nine years. There were 36 cases of pyelitis and pyelonephrosis, 9 cases of hydronephrosis, all in association with prostatic disease, and 6 of nephrolithiasis; 27 of all these conditions were in the non-hypertrophic class.

In certainly three-fourths of all cases examined sclerosis of the renal arteries, varying in degree and extent, was present. In certain cases it was most marked in the arcuate arteries, in others in the interlobular and the glomerular branches, and in others all were affected. The evident condition in these arteries was atrophy and destruction of the media with increase in the intima. In some arteries it was distinctly focal, in others the entire wall was equally affected, the artery represented by a small lumen surrounded by a hyaline mass, the media having completely disappeared. The elastica in most cases shared the fate of the muscularis, in others the elastic lamina was split and formed a series of concentric circles in the hyaline masses. As far as it was possible to determine, the atrophy and destruction of the media was primary, always more marked near the internal surface, and the changes in the intima were proportional to the medial injury. The caliber generally seemed reduced in size, often irregular, but, of course, such examination can give us no information of the caliber during life. Associated with these arterial changes there were glomerular changes consisting in thickening of the capillary walls of single vessels or groups, gradually involving the entire structure. The minute arteries were

affected to a much greater degree than the main stem, which was often free from lesion. It is impossible to see these vascular lesions, producing, as they must, interference with the circulation and thereby disturbing nutrition and function, without holding them accountable for at least a part of the renal change. There are certain conditions, however, which make the matter uncertain. The coronary arteries of the heart are very generally affected in old age, and although fibrous myocarditis is often present, no definite relation exists between this and the vascular disease. It is further true that the main coronary vessels are affected to a greater degree than the small penetrating branches, while the reverse is true in the kidneys. In the arteriosclerosis of younger individuals there may be extensive changes in the renal arteries without the lesions so characteristic of the old. Old dogs, in whom arteriosclerosis can practically be excluded, have atrophic lesions of the kidneys involving both tubules and glomeruli, but they differ in kind from the changes in the human kidney. No vessels in the body are so free from disease as in the liver, and yet here there is in old age atrophy of parenchyma and increase in fibrous tissue. It is absurd to attempt to refer old age to arteriosclerosis, and yet anyone studying these kidneys, in which the vascular lesions are so general and so striking, would almost certainly regard them as the primary and essential factor.

Through the courtesy of Dr. H. A. Christian I am enabled to give the records of the blood pressure in the Peter Bent Brigham Hospital cases, omitting one case of very high pressure due to intracranial tumor.

HYPERTROPHIC CASES

Male		Female		General Average	
Systolic	Diastolic	Systolic	Diastolic	Systolic	Diastolic
160	87	153	90	158	88

Extremes

(Disregarding one case of cerebral tumor.)

	Systolic	Diastolic
High	235	160
Low	90	40

NON-HYPERTROPHIC CASES

Male		Female		General Average	
Systolic	Diastolic	Systolic	Diastolic	Systolic	Diastolic
127	78	134	77	130	78

Extremes

	Systolic	Diastolic
High	195	100
Low	60	30

These figures do not differ essentially from those given by others. Woley gives 138 systolic as the average at the ages sixty to sixty-five. Weldt has found that from sixty to ninety years the systolic pressure increases from 137 to 190, but after ninety the pressure gradually falls.

Conclusions. The main interest which has come from the study of these cases is the demonstration of the great frequency of heart hypertrophy in old people. I regard it as pathological, due to some unusual conditions, and not as a part of the physiological changes of age. It is as difficult to give any adequate explanation of heart hypertrophy in the old as it is to explain the condition at any period of life. The whole question of muscular hypertrophy is obscure. The mechanical explanation that the heart meets continued opposition to the passage of blood through or from it by acquiring greater power through increase of muscular substance, and that this is the essential cause of all hypertrophies, though no longer so firmly held as it was twenty-five years ago, is adequate in certain cases. Hypertrophy does take place in all cases of aortic stenosis and insufficiency at any period of life. It also takes place in certain cases where the peripheral resistance is increased. It takes place, I think, always in the cases of subacute and chronic glomerulonephropathy, in which cases there is a maximum interference with the circulation through the kidney. The mere reduction in the amount of renal tissue even in cases in which, like hydronephrosis, there would seem to be circulatory obstruction, may or may not be associated with hypertrophy. The influence of arteriosclerosis of the aorta and its main branches in producing hypertrophy may be disregarded. In these cases it was always present, and there was no relation to heart hypertrophy in the degree and extent of the arterial changes. When I began the study of these cases I thought there was a relation between heart hypertrophy and that type of arteriosclerosis of the renal arteries in which the interlobular arteries and the glomerular branches were affected. For a time I was successful in naming the condition of the heart from the examination of the kidney sections, but finally mistakes were so frequent as to show that, while this relation is frequent, it is far from being universal. It has been assumed by some, notably by MacKenzie, that the increased blood pressure of age is due to reduction of the capillary area of the cutaneous circulation, but though it is evident from the senile

changes of the skin that there is a reduction of the capillary area, it is as evident in the nonhypertrophies as in the hypertrophies. There is need in all these obscure cases of hypertrophy of the heart of a much more thorough study of terminal arteries and capillaries than was possible in the cases here reported. The heart in old age, as in all periods of life, is a good mechanism, and it does not fail, but is even capable of increasing its capacity for work when the other machines of the body are slacking in their efforts.

EPIDEMIOLOGY OF POLIOMYELITIS

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THE severe epidemics of poliomyelitis of the past fifteen years have established a new world record. They have served also to bring into the foreground of medical discussion the epidemiology of the disease.

The series of epidemics alluded to may be considered to date from the Norwegian and Swedish outbreaks of 1903 to 1905. Previous to those occurrences, occasional foci of cases of poliomyelitis appeared in widely separated localities in Europe and the United States, but no wide spread of the disease resulted from those foci.

The Norwegian and Swedish epidemics, and particularly the epidemic of 1905, appear to be the immediate forerunners of the pandemic which prevailed from 1907 to 1909 in Europe and America. Subsequently the disease reappeared in epidemic form in Scandinavia in 1911 and 1913. In the United States the pandemic of 1907 to 1909 left behind either small local foci of poliomyelitis, or, what was more frequent, conditions favoring a greater incidence of the sporadic disease than had previously been noted.

This was, in brief, the situation until 1916, when an outburst of the disease of unparalleled severity overwhelmed the North Atlantic region of the United States. The storm center of the epidemic wave was New York City and the adjacent regions of New York State, Connecticut, and Massachusetts. The epidemic was not confined to the Northeastern States, but in far less degree involved the Middle and Southern, and even the far Western States. The reported cases in New York State as a whole exceeded 20,000; but it is improbable that even that great figure really includes all the cases which arose between May, when the first five cases were reported in New York City, and November, at which time the usual incidence seems to have been re-established. The diagram (Fig. 1) gives an approximate indication of the distribution of the epidemic foci of 1916.

As registration is unequal in different sections of the country, it is to be assumed that the occurrences are under rather than overstated.

But what is particularly remarkable is the fact that, notwithstanding the unequaled intensity of the 1916 outbreak in the Atlantic coast region and partial dissemination of the malady in the interior of the United States, the greater part of the country escaped attack, and the disease failed to reappear in force in 1917 or subsequently up to the present writing (April, 1919). In other words, the very

Shaded Areas Show Localities Particularly Involved in the Poliomyelitis Epidemic of 1916.

fury of the epidemic disease seems to have brought about rapid exhaustion of its striking power.

This last phenomenon is met with in some degree with epidemics generally; it is the peculiarly impressive quality of this instance which specially arrests attention. It is of interest to observe that in New York City, where by far the greatest number of cases was massed together, the incidence was 1.59 per thousand of population, and 83 per cent of all reported cases were in children under five years of age. In many parts of the United States the attack rate was far below that of New York City. And yet the epidemic abated during the autumn of 1916 and has not yet recurred. Hence it would

seem that the factors governing the attack rate and those affecting the rise of the epidemics may be quite dissimilar.

In seeking an explanation for the attack rate, we easily fall back upon those general, if vague, principles of susceptibility which appear everywhere to operate in promoting or preventing infection; or we incline towards the notion, as yet quite hypothetical, of a state of rapid and wide immunization of communities through inappreciably mild attacks of disease. The relatively recent knowledge and implications of the carrier state have made this idea easily acceptable.

The conception that the incidents leading to the peculiar curve of the epidemics of poliomyelitis are brought about by wide dissemination of the microbic agent of the disease through abortive cases and healthy carriers has been several times advanced, for example by Kling, Pettersson, and Wernstedt, (1) who studied the Swedish epidemics of the years between 1905 to 1911, and by Wernstedt, (2) who studied the epidemic of 1911. It has again been invoked by Lavinder, Freeman, and Frost, (3) who made an epidemiological study of the 1916 epidemic in the Northeastern part of the United States. The latter authors state in effect that an incidence of one to three recognized cases per thousand, or even less, immunizes the general population to such an extent that the outbreaks decline spontaneously, due to exhaustion or thinning out of the infectible material. In like manner, they conceive that communities visited by a few cases may be preserved from a severe visitation at a later period at which the epidemic is prevailing elsewhere in fresh territory.

Our views on the epidemiology of poliomyelitis are based largely on statistical observations and very little on experimentally verifiable data. Mere statistical observations have led to the notion so generally accepted that poliomyelitis is strictly a seasonal—late summer and autumn—disease. The fact is that outbreaks of some dimensions have repeatedly taken place in the winter in Scandinavia; recently a midwinter outbreak occurred in the United States in and about Fairmont, W. Va. Epidemic poliomyelitis and epidemic cerebrospinal meningitis have been not infrequently confounded with each other. As the latter disease tends to prevail in the winter and early spring months, a more precise clinical study might not improbably show that at times the latter is mistaken for the former.

II. It is commonly supposed that epidemics of poliomyelitis arise at given places through the importation from another region, near or remote, of specimens of the microbic agent or virus of heightened virulence. We possess, indeed, conclusive evidence that this virus undergoes a remarkable increase in activity through mere passage from individual to individual.

That is, by successive passages of human strains of the virus through monkeys, a high degree of virulence may be attained for that species. How great the changes are that take place can be inferred only, since in the inoculation of filtered extracts of the nervous organs we cannot actually measure the number of micro-organisms introduced. The rise in virulence is shown not only by the smaller effective dose, but also by the circumstance that while at the beginning of the adaptation the proportion of monkeys developing paralysis is smaller and the number of recoveries after paralysis larger than at a later period, once the adaptation has been accomplished all the animals inoculated tend to become paralyzed and succumb to the disease.

Once acquired, this state of high virulence is retained over a long period of time; whether it becomes a fixed quality has not hitherto been known. This latter point is of fundamental importance. It now appears (4) that a particular strain of the poliomyelitic virus which had acquired high virulence and maintained it for a period of three years, during which it was passed successively through *macacus rhesus* monkeys, had undergone successive deterioration of activity, until it about returned to the degree of infecting power corresponding to that which it possessed in the original human material.

It is possible to apply this experimental demonstration to the interpretation of the salient epidemiological phenomena of poliomyelitis. Thus, at the outset, the virus of poliomyelitis possesses relatively weak pathogenic action in monkeys. By means of a few passages, the infective power rises and soon a maximum is reached which endures for some time. Ultimately the infective power falls off and soon becomes greatly diminished, so that finally the power is no greater than at the outset. This succession of changes dependent on alterations of virulence finds a counterpart in the phenomena noted during the rise, persistence, then fall of the number of cases that constitute epidemics of the disease. Moreover, the fluctuations in

virulence depend, as far as can be seen, on causes acting on the virus from within the body of the animals, which causes, whatever their nature, operate to produce a cycle of activity indicated by rise, fixation, and decline in infecting power. And this is the cycle, apparently, that many epidemics pass through in the course of their appearance and disappearance.

That the virus of poliomyelitis is communicated by personal contact is now generally admitted; and that it occurs in the nasopharynx, which constitutes the chief locus of ingress and egress to and from the body, is also conceded. The fact that the virus has in a very few instances been detected in healthy persons who have been in intimate contact with early cases of poliomyelitis, and even in certain individuals who have recovered from the acute effects of the disease, has led to the generalization that, like some other diseases of bacterial origin, and notably epidemic meningitis, healthy and chronic carriers of the virus are frequent. This view has received its main support from Kling, Pettersson, and Wernstedt. A critical analysis of the basis of their contention fails, however, to carry conviction.

The inadequacy of their data is made more probable by the experiments made with excised pharyngeal and nasal tissues taken either post-mortem or removed surgically during life. (*5*) The two sets of tissues, those removed at autopsy and those removed during life, differed in one essential respect. The former came from cases of poliomyelitis in the first week, and the latter later in the course of the disease. On the basis of infectivity the deduction seemed warranted that the nasal and pharyngeal mucosæ of persons succumbing to polyomyelitis during the first ten days of the disease probably regularly contain the virus, while the virus diminishes relatively quickly as the disease progresses, except in rare instances; and it is unusual for a carrier state to be developed.

Available evidence proves that healthy carriers of the virus occur. We do not, however, possess data which indicate the frequency with which carriage arises. The fact that even after a severe and wide epidemic, such as occurred in the United States in 1916, the disease may virtually disappear in two or three years, points to the probability that enduring carriers of the virus, whether healthy or chronic, are of exceptional occurrence.

To the two factors, namely, that the microbic agent or virus of poliomyelitis fluctuates in virulence and tends rapidly to disappear from the upper respiratory mucous membrane during convalescence, may be attributed certain striking features of the epidemiological history of the disease.

BIBLIOGRAPHY

1. Kling, C., Pettersson, A., and Wernstedt, W., "Communications de l'Institut Médical de l'État à Stockholm," 1912, 261.
2. Wernstedt, W., ibid., 264.
3. Lavinder, C. H., Freeman, A. W., and Frost, W. H., *Pub. Health Bull.*, Washington, No. 91, July, 1918.
4. Flexner, S., Clark, P. F., and Amoss, H. L., *J. Exper. M.*, 1914, XIX, 45.
5. Flexner, S., and Amoss, H. L., *J. Exper. M.*, 1919, XXIX, 379.

HEMANGIOENDOTHELIOMA OF THE LIVER IN THE INFANT, AND SO-CALLED ANGIOSARCOMA

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PRIMARY adenoma, cavernoma, and sarcoma of the liver are not unusually rare even in early life. Steffen's collection of tumors in childhood, (1) Knott's (2) article on primary sarcoma of the liver with protocols of seventy cases, and numerous isolated case reports from French, Russian, and especially Italian pathologists bring the occurrence of these growths quite outside the range of singularity.

The simple or solitary angiomas of the liver, though relatively frequent in adult autopsies, are far from common in children; Kaufmann, (3) Michailow, (4) Steffen, (1) Gatewood (5) and others have reported these formations, but Gatewood could find less than a score in all.

The rarest of all primary tumors of the liver in infancy are the hemangioendotheliomas; almost as infrequent are hemangiosarcomas. That angiomas of the skin and multiple angiomas of the liver may assume an endothelial sarcoma type has been pointed out in adult cases by Dutton (6) and Fischer (7). But although the rapidly growing hemangioendotheliomas of the liver in infants have been named by some observers endotheliomas and by others sarcomas, they are so similar in history, clinical course, and gross anatomy as to constitute a distinct clinical entity among the disorders of early life sufficient to strengthen still further the anatomical evidence in adult tumors of the identity of the two conditions.

The following case history from the Pediatric Department of Providence Hospital, Washington, D. C., is typical.

Case No. 4620. Male child three months old, referred by Dr. R. Pyles for obstinate constipation suggesting intestinal obstruction. Was born at full term and breast fed until two weeks before entry. Constipation began

when two months old; enlargement of abdomen also noticeable at this time. No bowel movement in last seventy-two hours.

Examination. Fairly well-nourished child, prominent abdomen, intestines distended. Liver edge irregular, 7 cm. below costal margin in mammary line. A mass in abdomen extending toward back reaching to iliac crest on right side. (Wassermann negative in both parents.)

Exploratory laparotomy by Dr. Harrison Crook showed a large liver, purplish in color with numerous nodules of varying size up to a marble. No intestinal adhesions were noted. Wound closed after hemorrhage was stopped by packing. Death occurred in twenty-four hours.

Autopsy by Drs. J. L. Glass and John A. Foote.

CASE. Fairly well-nourished boy. Abdomen prominent. Right lung small and more compressed than left. Diaphragm pushed upward to level of third rib on right by liver. Lungs, kidneys, and spleen normal.

Liver, weight 740 grams. After hardening was 22 cm. by 13 cm. by 6 cm. It was mottled red in color. Superior and inferior surfaces were covered by about seventy-five nodules varying in size from a mustard seed to a walnut. Nodules were round, confluent in some areas, and were lighter in color at the summit of each boss. Section showed these nodules throughout the liver substance. When cut the nodules had a dark center with a capsule-like circle of lighter tissue outside.

Microscopic Examination. Connective tissue of interlobular septa increased, especially near the bile ducts. Liver cells stain irregularly, show vacuoles and are distorted in certain areas. Some cells have unusually large nuclei. Compressed liver cells and fibrous tissue form rings in areas corresponding to blood vessels with atrophic liver cells outside these rings. The contents of these nodules are red blood cells, a few white cells and debris, with more or less incomplete lining envelopes of large endothelial cells in the smaller nodules, sometimes in more than one layer. Outside the endothelium and in lacunæ in the fibrous septa corresponding to the wall of these vessel nodules are nests of cells, some of which resemble degenerated liver cells, others the endothelial lining. These endothelial cells are somewhat rounded with very large, oval, deeply staining nuclei, mitotic figures and chromatin showing in abundance. In observing the smaller vessels they are found to be literally choked with endothelial cells, double and triple layers of cells being seen in some fields. These vessels merge into masses of small round cells in the connective tissue trabeculæ. The smaller nodules show typical tumor formation of cells resembling myxosarcoma, a sharp line of demarcation of fibrous tissue showing between these areas and abnormal liver tissue surrounding them.

Section of spleen, lungs, heart, and stomach show no metastases.

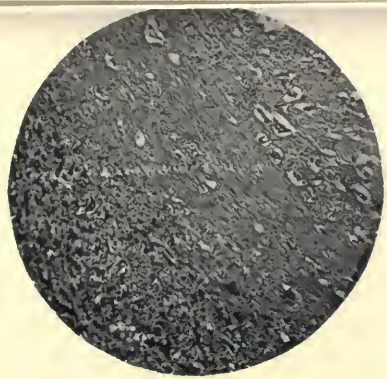

FIG. 1. Edge of Nodule, Showing Fibrous Tissue and Lacunæ. 50 × 1.

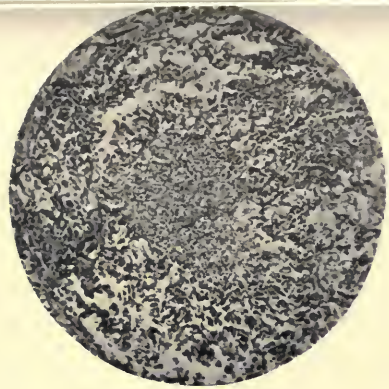

FIG. 2. Contents of Nodule, Showing Embryonic Type of Cells. 50 × 1.

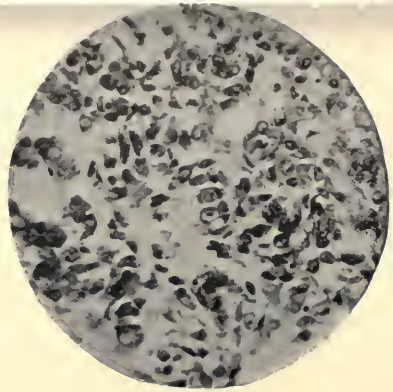

FIG. 3. Typical Cells in Center of Nodule. 200 × 1.

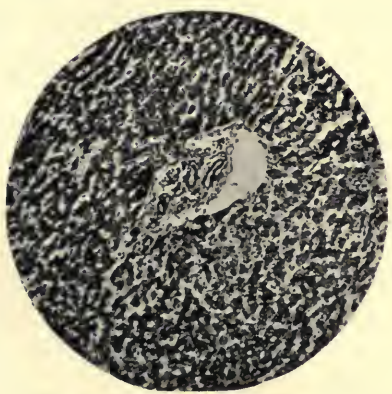

FIG. 4. Interlobular Septum with Blood Vessels. 60 × 1.

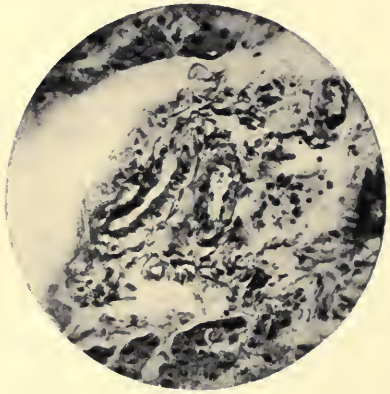

FIG. 5. Smaller Blood Vessels in Septum Showing Swelling and Proliferation of Endothelium. 200 × 1.

HEMANGIOENDOTHELIOMA OF THE LIVER IN THE INFANT. (FOOTE.)
(Microphotographs by Martin, from Sections by Lieut. Z. Bolin, U. S. A.)

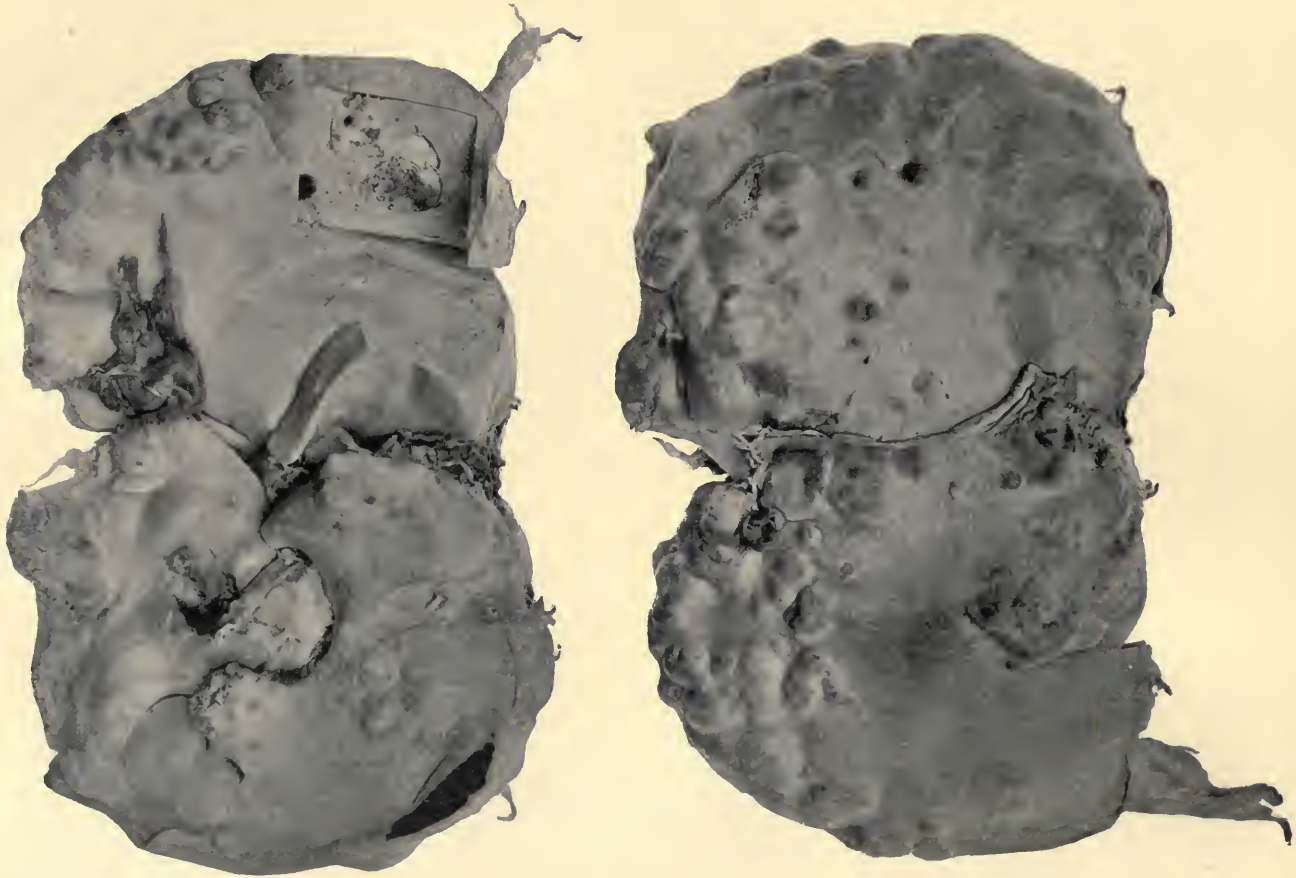

FIG. 6. Inferior Surface with Cut Section Showing Nodules.

FIG. 7. Superior Surface.

HEMANGIOENDOTHELIOMA OF THE LIVER IN THE INFANT.

(Photographs of hardened specimen by Martin, National Geographic Society.)

Diagnosis. Hemangioendotheliosarcoma.

Veeder and Austin (8) in their report of the first American case of hemangioendothelioma in an infant in 1912 could find only three others in the literature at that time. Stern (9) reported a typical case in 1915, bringing the total up to five. To this should be added in all likelihood the cases reported as sarcomas by Lendrop[1] in 1893, de Haan[2] in 1903 and Parker,[3] as well as the one just reported by the writer. A case reported by Bondy[4] in 1911 as angiosarcoma without histological details was similar in gross anatomy and clinical findings. This gives in all nine cases of enlargement of the liver in children appearing shortly after birth, increasing rapidly about the third month, with no jaundice, little disturbance of nutrition and resulting in death from progressive weakness usually about the fifth month. The liver in all cases is enlarged and nodulated, the nodules made up of dilated blood vessels. A proliferation of endothelium is made out in every case where a detailed histological study has been given. The case of Sawyer (10) abstracted by Veeder and Austin is not included in the following summary, since it was far from typical and autopsy revealed other conditions which may have caused death.

Reported by	Clinical History	Gross Anatomy of the Liver	Histology
Chervinsky. *Arch. d. Phys. norm. et path.* 1885, VI, 553. Diagnosis, endothelioma.	Abdominal enlargement noticed at six weeks. Growth very rapid. Death at six months from general exhaustion. No jaundice.	Weight, 943 grams. Very large liver. Purplish red. Many nodules on surface varying in size from a pea to an egg. Nodules on section showed a red center surrounded by white rings, some showing fibrous bands running to the periphery.	Blood spaces lined with endothelial cells in more than one layer in places, and containing red and white blood cells and debris. Capsule about nodule made up of compressed cellular and fibrous tissue. Parts of liver show fatty degeneration in filtration and an increase of perilobular tissue.

[1] See Summary of Malignant Angiomas, etc., p. 938.
[2] Ibid., p. 938.
[3] Ibid., p. 938.
[4] Ibid., p. 938.

Reported by	Clinical History	Gross Anatomy of the Liver	Histology
Bruchanow. *Zeitschr. f. Heilk.*, 1889, XX, 431. Diagnosis, endothelioma.	Infant, fifteen weeks. Showed angiomas of the skin and an abdominal tumor. Death from exhaustion at fifteen weeks. No jaundice.	Weight, 710 grams. Dark red in color. Nodulated. Nodules vary in size from pea to hen's egg. On section are red in center and whiter at periphery. An increase of interlobular tissue.	Essentially the same as Chervinsky's case.
Lendrop. *Hospitalstidende*, 1893, p. 217. Diagnosis, sarcoma.	Infant, female, four months old. Large mass in abdomen. No jaundice.	Weight, 1625 grams. Enormous liver, nodular and dark red in color. Nodules of varying sizes up to a walnut. Section shows nodules throughout entire liver.	Nodules contain round cells originating in endothelium of interacinous blood vessels and penetrating into the veins. Liver cells compressed and degenerated.
De Haan. *Ziegler's Beitr. z. Path. Anat.*, 1903, XXXIV, Heft 2, 215. Diagnosis, sarcoma.	Child four months old. Large nodular mass made out in abdomen. No jaundice.	Weight, 867 grams. Liver dark and covered with nodules of all sizes showing lighter under a smooth capsule, some confluent. Section shows them throughout liver.	Nodules contain many round cells with deeply staining nuclei. Blood-vessels dilated and choked with large endothelial cells. Tumor masses of similar cells. Growth due to proliferation of capillary endothelium.
Parker. *Trans. Path. Soc.*, London, XXXI, 290. Diagnosis, sarcoma.	Infant constipated, died from weakness aged five weeks. Abdominal swelling noted at three weeks. No jaundice.	Large liver nodulated with millet seed to walnut-sized masses. Contents whitish at edge, darker at center.	Vessels enlarged and distended. Liver shows many small round cells, especially near small vessels.
Bondy. *Jrn. A. M. A.*, 1911, LVI, 12, 873. Diagnosis, sarcoma.	Increase in girth noticed at three weeks due to mass in liver region. Exploratory laparotomy performed. Child lived to three and one-half months, dying from weakness. No autopsy, but portion of liver removed at operation.	Purplish liver seen at operation occupying three-quarters of abdominal cavity. Surface covered with nodules.	No histological details given. A diagnosis of angio-sarcoma made by pathologist.

Reported by	Clinical History	Gross Anatomy of the Liver	Histology
Veeder and Austin. *Am. Jrn. Med. Sc.*, 1912–13, CXLIII, 102–107. Diagnosis, endothelioma.	Female child showing enlargement of abdomen progressive since birth. Brought to hospital at ten weeks. Nodular mass in liver region. Child grew weaker, dying a week later.	Liver enlarged to umbilicus. Many reddish purple nodules varying in size from a millet seed to a marble. On section show a red center surrounded by a lighter zone. These are found throughout liver.	Nodules made of dilated vessels. Blood spaces packed with red cells. Endothelium sometimes in double layers. Endothelial cells have large oval nuclei. Around each nodule an irregular capsule of connective tissue and compressed liver cells. Capsule of Glisson shows overgrowth of connective tissue. Liver cells show fatty changes.
Stern. *Arch. of Diag.*, 1915, VIII, 72–73. Diagnosis, hemangioma.	At six weeks brought to hospital for feeding advice. Nodular liver mass noted. *x*-ray showed tumor extending to pelvis.	Child left hospital and died a few days later of weakness. Only a partial abdominal autopsy. Large reddish-purple nodular liver.	Portion of liver removed showed multiple angiomatous cavities lined with many endothelial cells.
Foote. 1918.	Child brought to hospital at three months for constipation. Enlargement of abdomen noted and a nodular mass made out in liver region. Operation showed purplish nodular liver. Considerable amount of bleeding from cut nodule. Child died within twenty-four hours.	Liver weight, 740 grams. Covered with nodules, about seventy-five, varying in size from a millet seed to a walnut. Section showed nodules throughout liver. Red centers with whiter areas surrounding them seen in each nodule.	Nodules packed with characteristic cells, red blood cells, and debris. The vessels show large endothelial cells in multiple layers. Vessel and nodule walls thickened and infiltrated with large round and oval nucleated cells. Capsule of Glisson increased in size of septa. Capillaries show endothelial proliferation merging in places to a mass of primitive round cells. Mitotic figures in nuclei.

In spite of the fact that no metastases can be demonstrated, the malignancy of these tumors cannot well be disputed. Adami, (11) after defining sarcoma and amplifying his definition, says in italics.

"Therefore . . . the actively growing tumors of transitional lepidic character have also from this standpoint to be included as sarcomatous."

That angiosarcoma of this type develops from within the vessel walls by endothelial proliferation is urged by Dutton (12) in his report of two angiomas of the skin in an eight-year-old child. His microphotographs show the same endothelial proliferation and histological pictures seen in the endothelial tumor of the liver reported by the writer and others. Fischer (13) has collected three cases of hemangioendothelioma of the liver of a malignant type in adults. In several beautiful plates he shows definitely the endothelial proliferation and infiltration down to the ultimate typical sarcoma structure of metamorphosed endothelial cells. He takes issue with Ribbert and maintains that these tumors develop rapidly by successive changes in contiguous apparently normal endothelial cells. "The tumor cells lie in normal anatomical relation to the endothelial tube, proving conclusively that the cells have originated in this location," he says. An embryonic type of liver endothelium, retaining even the embryonic function of hematopoiesis as described by Borst, Schwalbe, and others, is responsible, in his opinion, for the rapid and peculiar growth of these remarkable tumors.

Many theories have been put forth to explain the origin of the simple angiomas and the hemangioendotheliomas of the liver. Chervinsky,[5] who was the first to describe hemangioendotheliomas of the liver in an infant, believed that these tumors were easily explained through the theory of fetal inclusion, a view also held by Pilliet. (14) Bruchanow (15) believed that the capillaries of the liver established an abnormal relationship to the rest of the liver, especially the liver cells, continuing their growth and development independently of the normal relationships of adjacent tissues. To both of these views Schmieden (16) objected that a simple growth or dilatation of vessels of the type described was no true blastoma formation, such angiomas being the result of the simple growth and dilatation of capillaries into budding masses of liver tissue which in the process of development had been cut off from the rest of the liver. Ribbert failed to inject the dilated vessels through the hepatic vein. According to Mallory's postulates, in true hemangioendothelioma it must be established that new blood vessels are formed and that the endothelial cells have proliferated.

All of these attempted explanations of the beginnings of these tumors go back to an abnormal developmental condition followed

[5] Chervinsky, see Summary of Malignant Angiomas, p. 937.

by an unrestrained growth and dilatation of the blood vessels. However, the rapid proliferation of the endothelium in the capillaries choking them and extending the process to larger vessels, with the resulting stasis and dilatation and infiltration of the vascular structure, is the characteristic picture of the end of this process, whatever its beginning may have been. The primitive type of cell seen in the endothelium of vessels with large nuclei rich in chromatin, showing rapid growth, and the clinical picture of rapidly growing liver-tumor without jaundice, accompanied by general weakness and terminating fatally, bear out to an unusual degree Adami's assertion that all tumors of this character must be considered as sarcomas. The histological evidence in the cases of Dutton, Fischer, and the writer shows that these growths are neither true benign hemangioendotheliomas nor typical angiosarcomas, but a malignant growth originating in the endothelium of the blood vessels forming no metastases, perhaps best described by the term *hemangioendotheliosarcoma* and seen characteristically in the liver of infants during the first few months of life.

BIBLIOGRAPHY

1. Steffen, A., "Die malignen Geschwulste im Kindesalter," Stuttgart, 1908.
2. Knott, Van B., *Surg., Gynec. & Obst.*, 1908, VII, 328–341.
3. Kauffmann, *Spezielle path. Anat.*, 1907, 579.
4. Michailow, *Arch. f. Kinderh.*, 1901, XXI, 291.
5. Gatewood, *Tr. Chicago Path. Soc.*, VIII, 311–316.
6. Dutton, J. E., *Liverpool Med.-Chir. J.*, 1898, XVIII, 369–376.
7. Fischer, B., *Frankfurt. Ztschr. f. Path., Wiesb.*, 1913, XII, 399–421.
8. Veeder and Austin, *Am. J. M. Sc.*, 1912–13, CXLIII, pp. 102–107.
9. Stern, A., *Arch. Diagn.*, 1915, VIII, 72–73.
10. Sawyer, *Rep. Soc. Study Dis. Child.*, Lond., 1906, VII, 19.
11. Adami, "Principles of Pathology," 1910, I, 762.
12. Ibid., 6.
13. Ibid., 7.
14. Pilliet, *Progrès Méd.*, XXIX, 50.
15. Bruchanow, *Ztschr. f. Heilk.*, 1889, XX, 431,
16. Schmieden, *Virchow's Arch. f. path. Anat.*, 1900, CLXL, p. 373.
17. *J. Exper. M.*, 1908, X, 575.

THE PRODUCTION OF AN ANTIHEMOLYSIN FOR THE HEMOLYSIN OF BACTERIUM WELCHII

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and
George Huntington Williams, M.D.
(From the Department of Bacteriology, School of Hygiene and Public Health, Johns Hopkins University)

IT has previously been shown by Ford and Lawrence that the whey from market milk, which decomposes after heating to 80° C. for twenty to thirty minutes, contains substances which dissolve the red blood corpuscles of a number of animals, and that these substances are produced in the milk by the multiplication of the "gas bacillus" of Welch and Nuttall. The hemolysin of this organism has been further shown to be independent of the acids produced in the milk, to be destroyed at about 60° C., to be precipitable by ethyl alcohol, and to be acted upon by the digestive ferments. For these reasons this blood-taking substance was placed in the group of bacterial hemolysins, and the destruction of blood by cultures of the gas bacillus was attributed to its activity, and not to the lactic and butyric acids which are produced by the organism in the decomposition of the ingredients of the milk. Subsequent investigation of the properties of milk cultures of the gas bacillus has confirmed our earlier observations and has added a number of other points of interest, especially the production of an antihemolysin to this substance.

Preparation of the Hemolysin. The hemolysin of the gas bacillus can be obtained from milk by the following method. Pure cultures of the organism are isolated from market milk by heating flasks containing about 300 c.c. to 80° C. for twenty to thirty minutes and incubating at 37° C. In the majority of samples so treated the "stormy fermentation" characteristic of this species appears in twenty-four to forty-eight hours. Transfers of the whey from such fermented samples to litmus milk tubes often gives pure cultures

after four to five transfers, owing to the rapid development of *Bacterium Welchii*, by virtue of which it overgrows nearly all other micro-organisms except certain acid-resistant streptococci. When the cultures do not become pure, the material may be run through rabbits by the usual methods, and pure cultures obtained from the heart's blood or liver. With such freshly isolated strains, large flasks of sterile milk containing about a liter are inoculated by pouring into them the entire contents of a twenty-four hour litmus milk culture of the organism, about 12 to 15 c.c. Such flasks of milk undergo violent fermentation within twenty-four to forty-eight hours. The grosser particles of curd are now removed by filter paper and the filtrate immediately neutralized by the addition of caustic potash. The filtration requires eighteen to twenty hours, during which time there is a further multiplication of the organisms, as is shown by an increase of activity. On subsequent neutralization an abundant gelatinous precipitate appears. This also may be removed by passing through filter paper. The fluid obtained is clear, rather viscid, yellowish brown in color. If not entirely free from bacteria it may finally be run through a Berkefeld candle. This final product of the milk culture of the gas bacillus has marked hemolytic properties, as shown by the following table:

TABLE I

HEMOLYTIC PROPERTIES OF FILTRATE FROM MILK CULTURE OF *Bacterium Welchii* TESTED ON RABBIT'S BLOOD

FILTRATE		RED BLOOD CORPUSCLE 5 PER CENT SUSPENSION		HEMOLYSIS
1 c.c.	+	1 c.c.	=	Complete
0·75 c.c.	+	1 c.c.	=	Complete
0·5 c.c.	+	1 c.c.	=	Complete
0·25 c.c.	+	1 c.c.	=	Complete
0·1 c.c.	+	1 c.c.	=	Complete
0·075 c.c.	+	1 c.c.	=	Complete
0·05 c.c.	+	1 c.c.	=	Complete
0·025 c.c.	+	1 c.c.	=	Complete
0·01 c.c.	+	1 c.c.	=	Negative
1 c.c. NaCl 0·75 per cent	+	1 c.c.	=	Negative

From this table it may be seen that 0.025 c.c. of the filtrate suffices to bring about complete solution of 1 c.c. of a 5 per cent suspension of rabbit's-blood corpuscles, representing a dilution of

1–40. This quantity may be taken as the hemolytic unit or the hemolyzing dose of the filtrate. Other preparations have been obtained in which the hemolyzing dose is somewhat higher, .01 c.c., but they are exceptional. The usual hemolytic unit is about 0.25 c.c. in a freshly prepared filtrate from a milk culture of the gas bacillus.

Preparation of an Antihemolysin. With the hemolytic filtrates as thus prepared a series of rabbits has now been successfully immunized. These animals were under treatment for some months, receiving gradually increasing doses of the hemolysin. During the treatment one animal developed a laboratory paralysis; while another became so badly infected that it had to be killed. The serum of the other four animals contained in all instances substances which completely neutralized the hemolysin of the gas bacillus in high dilution. This is shown in the following table:

TABLE II

STRENGTH OF ANTIHEMOLYSIN IN THE SERUM OF RABBIT IMMUNIZED WITH THE HEMOLYSIN OF *Bacterium Welchii* TITRATED AGANIST ONE HEMOLYTIC UNIT REPRESENTED BY 0.1 C.C. OF THE FILTRATE USED

FILTRATE	SERUM	BLOOD SUSPENSION 5 PER CENT	PROTECTION
0·1 c.c.	+ 0·1 c.c. +	1 c.c. =	Complete
0·1 c.c.	+ 0·06 c.c. +	1 c.c. =	Complete
0·1 c.c.	+ 0·04 c.c. +	1 c.c. =	Complete
0·1 c.c.	+ 0·02 c.c. +	1 c.c. =	Complete
0·1 c.c.	+ 0·01 c.c. +	1 c.c. =	Complete
0·1 c.c.	+ 0·006 c.c. +	1 c.c. =	Complete
0·1 c.c.	+ 0·004 c.c. +	1 c.c. =	Complete
0·1 c.c.	+ 0·002 c.c. +	1 c.c. =	Complete
0·1 c.c.	+ 0·001 c.c. +	1 c.c. =	Complete
0·1 c.c.	+ 0·0008 c.c. +	1 c.c. =	Complete
0·1 c.c.	+ 0·0006 c.c. +	1 c.c. =	Partial
0·1 c.c.	+ 0·0004 c.c. +	1 c.c. =	Hemolysis
0·1 c.c.	+ 0·0002 c.c. +	1 c.c. =	Hemolysis
0·1 c.c.	+ 0·0001 c.c. +	1 c.c. =	Hemolysis
Control	+ 1 c.c. NaCl 0.75%	1 c.c. =	Negative
0·1 c.c.	+ 1 c.c. NaCl 0.75%	1 c.c. =	Hemolysis

Complete protection against one hemolytic unit is thus afforded by .0008 c.c. of the serum, or a dilution of 1–1250. Normal serum prevents hemolysis only when used in large quantities, never beyond a dilution of 1–10. We thus have an artificial or an immune antihemolysin of a strength far beyond that of the antihemolysin of the

normal serum. The usual strength of the immune antihemolysin was about 1–1000.

Conclusion. By the immunization of animals with gradually increasing doses of the hemolysin of *Bacterium Welchii* we have now produced an antihemolysin of a strength of 1–1000 to 1–1280. The production of this substance offers the final proof of the opinion previously expressed, and definitely places the hemolysin of the gas bacillus in the groups of bacterial hemolysins capable of acting as antigens.

SYMPTOMLESS OBLITERATION OF THE SUPERIOR VENA CAVA

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CASES of obstruction of the superior vena cava resulting from compression of the vein from without by an aneurysm or by enlarged glands, whether due to tuberculosis, sarcoma, or Hodgkin's disease, and characterized by marked dilatation of the superficial thoracic and abdominal veins, with the venous flow from above downwards, are comparatively rare. Still more uncommon are those cases in which the obstruction is believed to be due to atresia of the lumen of the superior vena cava by fibrous tissue following extension of a mediastinitis to the vein, resulting in its partial or complete obstruction. The following case, not confirmed by autopsy unfortunately, appeared to belong to the latter group. It was of additional interest, owing to the fact that the patient appeared to have no symptoms directly referable to the venous obstruction, those from which he did suffer apparently being due to the myocardial insufficiency from which he suffered.

S. M., Med. No. 37,608, colored, male, married, age forty-five years, was admitted to the Johns Hopkins Hospital on March 21, 1917, having been under the observation of Dr. J. Hall Pleasants and the writer in the Medical Dispensary since March 13th. His complaint was shortness of breath and weakness of the heart.

The family history was unimportant, with the exception that his wife had had two miscarriages. The patient had mumps at ten years of age and measles at seventeen. There was no history of any of the other acute specific fevers. Between the ages of twelve and fifteen he had several mild attacks of arthritis, however, which incapacitated him for only a day or two at a time. There was no history of tonsillitis.

He performed hard manual labor, and for some time before admission had been an oyster-dredger on the Chesapeake Bay. Although for the past ten years he had experienced some palpitation of the heart on exertion, he had been able to perform hard labor up to two years before admission.

PHOTOGRAPH OF PATIENT, SHOWING MARKED DILATATION OF THE THORACIC AND ABDOMINAL VEINS, THE VENOUS CURRENT BEING FROM ABOVE DOWNWARDS.

No history of any venereal infection was elicited, notwithstanding the subsequent findings. He chewed tobacco moderately, and rarely took alcohol in any form. His greatest weight at any time had been 160 pounds.

For a good many years, at least ten or fifteen, he has observed enlarged veins over the front of the chest and abdomen. He had never experienced any pain over the upper segment of the chest.

The symptoms for which the patient was admitted began about two years previously. The onset was apparently rather abrupt, with a sense of weakness and dizziness while on the street, and he was taken to the Mercy Hospital, Baltimore, from the authorities of which the following statement was obtained: "Patient found unconscious on street by police and brought to Mercy Hospital, March 23, 1915. Diagnosis at that time, myocarditis, arrhythmia, and acute dilatation of the heart. Patient discharged April 1, 1915, in good condition."

The patient states that he had never experienced any shortness of breath previous to this attack. The day of the attack he had been carrying bags of grain which he thought weighed 75 pounds each. While he never noticed any swelling of the feet, he observed shortly after this attack that his face would be swollen after a night's rest, clearing up during the day.

Following his first admission to the Mercy Hospital he was readmitted for one week in July, 1915, and again for two weeks in October, 1915. The symptoms were similar to those in the first attack. From October, 1915, up to the time of his admission to the Johns Hopkins Hospital, the patient had not been able to perform hard labor, owing to shortness of breath and palpitation of the heart, although he had not been confined to bed for any length of time. He had not complained of upper thoracic pain and had had no cough.

Physical Examination. The patient was a well-nourished, fairly muscular colored man, weighing 147 pounds. While at rest there was no dyspnea. On baring the trunk, the outstanding features were two markedly dilated venous trunks about the size of one's index finger, extending down each side of the sternum and anastamosing with the superficial epigastric veins and disappearing at the level of Poupart's ligament, as seen in the accompanying photograph. The current of blood was from above downwards. The jugular veins were considerably distended, as were those also over the shoulders and upper arms. There was no evident cyanosis nor any definite turgescence of the face.

The examination of the radials showed them to be equal on the two sides; some irregularity from "ventricular premature systole" as demonstrated in the Heart Station by Dr. M. W. Brown. No definite thickening of the vessel walls. Pulse rate during observation was between 72 and 130

per minute. The blood pressure was low, the systolic ranging between 94 and 110 and diastolic between 72 and 85.

The pupils were equal. Ophthalmoscopic examination showed a little tortuosity of the retinal arteries. Veins a little full. Eyelids a trifle puffy. Conjunctivæ a little injected.

The lungs were clear by the ordinary methods of examination, with the exception of a few medium moist râles at the bases.

On March 21, 1917, Dr. Theodore Janeway made the following note: "Enlargement of superficial veins over lower thorax and upper abdomen. Blood current from above downwards. Point of maximum impulse diffuse and well inside the mammillary line. The relative cardiac dullness extends 12 cm. to the left in the fifth interspace and 8 cm. to the right at the level of the fourth interspace. Relative mediastinal dullness reaches 2.5 cm. to right and 6 cm. to left at the level of the first interspace. No definite lift of the upper sternum. Presystolic gallop at the apex. The mitral first sound is followed by a loud, rather harsh systolic murmur transmitted to the axilla, but not widely over the precordium. It is heard in the back below the angle of the scapula. Aortic second sound is not snapping. Pulmonic second a little accentuated. No impulse felt in episternal notch. No tracheal tug.

"Pupils equal and react to light and accommodation. Pulses equal and regular. Vessel walls not especially thickened. Liver just below the costal margin. Spleen not palpable. No edema of legs. Deep reflexes present, but reduced.

"Impression: Myocardial disease with relative mitral insufficiency. Probably syphilis of the aorta, but no evidence of aneuryism. Apparent obstruction of the superior vena cava, either partial or above azygos vein."

The laryngoscopic report by Dr. Chisolm was as follows: "Cords approximate fairly well, but there is definite weakness of the right cord, which is partially compensated by over-adduction of the left cord."

The blood Wassermann reaction was quadruple positive.

The complement fixation test of the blood was positive for tuberculosis.

The report on the roentgenogram of the chest was as follows: Dilated heart and aorta. Infiltration of both lungs, especially the right. Interlobular pleurisy on both sides. Lung condition suggests that these changes are tuberculous.

Fluoroscopic report: Dilated aorta, moderate in size. The pulsations are quite feeble. The heart is pulsating very slowly and there are pleural adhesions in right lung. Heart is enlarged.

The full blood count revealed nothing worthy of comment.

The urine showed an occasional trace of albumin, but no casts.

The temperature was practically normal throughout, with the exception of a slight elevation following a diarsenol injection.

The therapy consisted of rest in bed, digitalis, mercurial inunctions, and an injection of 0.2 mgm. of diarsenol.

The patient was discharged on April 19, 1917, only slightly improved. He insisted, against advice, on returning to his work as an oyster-dredger, but with instructions to return to the Medical Dispensary for observation. He failed to do so, and repeated efforts to trace the patient have been unsuccessful, so that it is impossible to report the subsequent history of the case.

This patient undoubtedly had obstruction of the superior vena cava, and a considerable part of the blood from the head and upper extremities must have been reaching the heart by way of the inferior vena cava, through the enormously dilated superficial thoracic and abdominal veins in which the flow was from above downwards. Without knowing whether the superior vena cava was obstructed below or at the level of the entrance of the vena azygos into it, it is impossible to say how much blood might be reaching the heart through the latter vein by means of its communications with the internal mammary veins by way of the intercostals.

The impression was that the symptoms of dyspnea and palpitation on exertion were due to the patient's myocardial insufficiency and not to his caval obstruction. The patient had noticed the enlarged superficial veins for ten to fifteen years, and it would appear that the collateral circulation that had been established had completely compensated for the caval obstruction. In a case reported by Vigoureux, sixteen years elapsed between the first signs of obstruction and death.

As this patient left the hospital improved from his myocardial insufficiency symptoms, and as the case did not come to autopsy, we have not the absolute information as to the nature and situation of the obstruction of the superior vena cava. Although the roentgenograms of the chest showed some diffuse dilatation of the arch of the aorta, the pulsation was feeble, and there was nothing to indicate pressure on the superior vena cava by a saccular aneurysm. Further, the absence of a tracheal tug, localized pulsation or lifting at the level of the sternum, led us to believe confidently that an aneurysm could be excluded. The absence of any extensive medias-

tinal shadow enabled us to eliminate a mediastinal tumor as the cause of pressure on the superior vena cava. By exclusion, we were forced to conclude that the caval obstruction was due to a mediastinitis, either syphilitic or tuberculous in origin, which had gradually involved the wall of the superior vena cava, possibly also causing a local thrombosis of the vessel, and eventually its complete atresia. The chances are in favor of there having been a syphilitic mediastinitis originating in the mediastinal glands, as the patient had a quadruple positive Wassermann. The possibility of the caval obstruction having been due to a tuberculous mediastinitis has to be entertained, owing to the fact that his blood gave a positive complement fixation test for the tubercle bacillus, and also from the fact that the roentgenograms showed nodules in both lungs. Clinically, however, the patient had no signs of active tuberculosis.

That obstruction of the superior vena cava evident enough to warrant a clinical diagnosis is rare is indicated by the fact that out of 41,346 medical admissions to the Johns Hopkins Hospital up to March 1, 1919, there have been only 10 cases. The present case, not confirmed by autopsy, and the remarkable case reported by Osler,[1] in which the autopsy showed complete atresia of the superior vena cava and the innominate vein, secondary to a fibrous mediastinitis probably tuberculous in origin, were the only 2 in which the vein was thought to be obstructed as a result of the extension of an inflammatory process from a chronic mediastinitis. Of the remaining 8, 4 were due to compression of the vein by an aneurysm, 1 by enlarged glands due to Hodgkin's disease, and 3 by mediastinal tumors.

Up to 1903 Osler had collected from the literature 29 cases of complete obstruction of the superior vena cava. Space will permit only a brief reference to the cases reported in the literature since that date. Search of the Index Medicus reveals only 11 references to obliteration or obstruction of the superior vena cava since 1903. In only 3 was there a fibrous obstruction of the vein. One of these, reported by A. Meyer, was congenital in origin, and both venæ cavæ were obliterated. This seems to be the only congenital case on record. The other 2 cases were reported by Comby, Vigoureux, and Collet, and A. M. Gossage. In the remaining 8 the obstruction was occasioned by pressure from without by an aneurysm or a tumor.

[1] Johns Hopkins Hosp. Bull., 1903, XIV, 169.

THE STUDY OF MORBID ANATOMY

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IT is desirable, from time to time, to take stock of the various ancillary subjects in relation to medicine, for the advancement of knowledge in neighbouring sciences and in special branches of medicine render previous notions of such relations obsolete; and unless the links are occasionally renewed our faith in the subject itself is liable to wane. This paper essays to review the special functions of morbid anatomy as a branch of pathology in relation to clinical medicine.

Morbid anatomy, studied with a broad outlook on disease and with the best methods of technique, is still the basis of teaching in clinical medicine, and one of the main opportunities for advance in knowledge. It is the means whereby pathological processes can be displayed in the clearest way and rendered useful both as a means of ascertaining their causation in individual patients and in order to reveal new causes and processes.

What is wanted is a return to the Hunterian outlook, a scheme in which all anatomical manifestations are used as stepping stones to the elucidation of disease. There is some danger, in the inevitable tendency to specialisation, to divorce morbid anatomy from clinical medicine. Necessarily there must be men who make it their sole study, men who spend their lives on the science itself, and who have no concern with practice. But wherever such men be, they should be in the closest touch with the clinicians and the clinical work of the hospitals they serve; they should be willing so to utilise their resources that the main purpose of medicine, the discovery and cure of disease, is facilitated and explored. From the clinical standpoint again, there must be a desire to utilise everything that may be established by the morbid anatomist for the benefit of the patient; there should be no such term as "pure clinician."

Formerly a good deal of what passed for pathology was of the "arm-chair" variety; a return of the Hunterian outlook would rid us of views that are insufficiently tested by either observation or

experiment. The soundest of the older physicians looked upon morbid anatomy as the centre point of all pathology, and notwithstanding the claims of bacteriological and experimental investigations this view is at the present time amply justified.

The amount of pathological learning demanded from students varies considerably in different universities and examining bodies. Though full courses are given, an adequate standard of knowledge is not always insisted upon even in those examinations that appear to require most training. Many physicians of the previous generation have acquired a knowledge of pathology only by careful reading and post-mortem observation during the practice of their profession. It must also be admitted that for the bulk of practitioners, pathological reasoning applied to clinical medicine is faulty. Few practitioners, however, can avoid having some system of pathology that will explain clinical events both to themselves and to their patients. The mental isolation and absence of pathological facilities in many types of practice tend to develop in each practitioner so situated a system of reasoning which often bears the flimsiest relation to facts. Teachers of morbid anatomy ought to set themselves to put into the student the sound principles of pathology which can always be demonstrated post-mortem and to refuse to countenance any hypotheses which are not based on such objective data. Such expressions as rheumatism, indigestion, neuralgia, would not imply a final diagnosis, but only a symptom of the physical condition which underlies it. Those who use these terms improperly are the victims of a system which does not provide an efficient pathological training, and they point the way to a more thorough training of the future student. The teaching of morbid anatomy should give him a philosophy that he can apply with benefit to his patients, and upon which he can subsequently build.

A widening of the scope and an increase of the pathological training is a matter of importance in the present training of students. It may be objected that the curriculum is already overburdened and that further loading of it would only defeat the purpose in view. But we must not fail to adjust our methods to modern conditions. The medical students of one hundred years ago were taught as apprentices by daily contact in their earliest days of studentship with the manifold expressions of disease in the patient. Throughout the

whole of their career they never lost touch with patients. Then came the introduction of the anatomical studies, later followed by chemistry, physics, biology, and physiology; and now in some universities we have an intermediate year devoted to pathology, pharmacology, and elementary physical diagnosis before the real hospital work begins. The special study of pathology as an introduction to medicine and surgery ought to be looked upon as a means of preparing the mind of the student to take more advantage of the years in the wards, so that when fully equipped for practice, he can interpret correctly the multitudinous phases of disease he has not seen while in hospital. It cannot be said that modern practitioners are any less skilled than those of former generations, notwithstanding the fact that their contact with patients during their years of training is actually less than formerly.

The subjects, apart from the fundamental ones of anatomy and physiology, that should form the immediate basis of clinical medicine are morbid anatomy, bacteriology, and experimental medicine, and of these the first is by far the most essential in training the mind to solve the problems of disease. The reason for this is that the greater bulk of diseased processes which the practitioner meets are gross, inflammations, local and general, vascular lesions, degenerative processes; all such as produce physical signs either at the site of or away from the lesion, and morbid anatomy is the only subject that will teach a student to think rightly in the terms of these processes. Wisdom in clinical medicine may be acquired by bedside study exclusively, but a lifetime spent in this way will fail to win the same skill of one helped by appropriate anatomical study of disease. That this is recognised by physicians who have the opportunity is proved by the fact that some of the best morbid anatomists are primarily physicians. On the other hand, some highly skilled physicians are ignorant of some anatomical processes; in the textbook of an eminent physician is a paragraph which indicates a failure to appreciate the fact that infarcts of the lung occur in cardiac disease, though he is aware of the symptoms in the patient and the anatomical appearances after death he fails to recognise the process. Properly conducted courses of morbid anatomy in the years of medical training should completely do away with such mistakes in the elements of pathology.

To picture to himself the anatomical lesions that underlie symptoms should be the habit of every practising doctor. He should be able to penetrate sufficiently deeply into the problems of disease as not to be satisfied with a diagnosis which merely connotes a symptom, as: congestion, bronchitis, indigestion, which imply nothing more than items in particular diseased conditions. To take only one of these terms, bronchitis, to the average practitioner means rhonchi heard on auscultation of the chest. The greater number of these cases are the result of an infection of the bronchial tubes, and rightly described as bronchitis, but it also occurs as an item in a number of other conditions, e.g., stasis in the lung vessels—increased secretion as in tetanus and uræmia, or as the result of malignant metastases of the lung. The term septic pneumonia again is a loose clinical term with no proper counterpart as a pathological process; it usually means a pneumonic process in the course of a septicæmia which is frequently a septic pulmonary embolism. Further, the term sapræmia does not correspond to any pathological condition known. In its anatomical features it is indistinguishable from mild septicæmia. In one of his addresses Sir William Osler has insisted on this, the anatomical view of the disease, in order to guard against the tendency to think that the patient who is the subject of a definite anatomical disease should ever be looked upon as if that disease did not exist.

The diagnosis of clinicians is in some diseases more accurate than is possible to mere naked-eye anatomy. On more than one occasion I have examined a uterus removed for carcinoma in which the diagnosis could not be confirmed with the naked eye, and yet histologically the diagnosis was upheld. Again a clinical diagnosis of carcinoma of the stomach was reversed to tubercular peritonitis at the post-mortem examination, but confirmed on the histological examination. The clinician deals with the complaints of patients which in some cases form extraordinarily delicate expressions of deranged function. This is specially noticed in the diagnosis of lesions in the central nervous system by the neurologist.

It is these considerations that force one to the conclusion that morbid anatomy during the student years is not studied with sufficient thoroughness and determination. On the average, the student spends two years studying mainly anatomy and physiology. In its

bearing on medicine and surgery pathological anatomy should occupy no less important place. What is required is, first, a recognition of its value, secondly, a reorganisation and an energetic prosecution of class work and demonstrations making it more of a principal than a subsidiary subject that in the minds of the student it has a tendency to become. If, however, morbid anatomy is to find its proper place in the medical study, not only must it explain the problems of the bedside, but it must constantly receive inspiration and help from clinical medicine. The morbid anatomist has frequently to lay bare the mistakes of a clinician in the post-mortem room, and this must never engender a self-sufficing attitude towards these problems as they appear in the wards, problems in which the most highly skilled are liable to error. It is necessary for the morbid anatomist occasionally to test his results by clinical methods. For instance, it is impossible to say of certain tumours of the breast whether they are malignant or not; this especially applies to tumours removed by the surgeon either wholly or in part and for which a diagnosis is asked. The only criterion that can guide the pathologist to an opinion is the amount and the degree of the hypertrophic process evident under the microscope. On this point the opinion formed from fixed preparations can never be final; the real test is the absence of recurrence in the body of the patient whose history would reveal the success or failure of the surgeon.

Morbid anatomical diagnosis should always if possible be ætiological; it is no help to the clinician to be told that there is fibrosis, necrosis, round-celled infiltration, and such like phenomena, unless those are preliminary to the expression of an opinion on the nature and if possible the cause of the tissue condition. Many lesions met with clinically cannot be fully explained by even the most searching anatomical investigation. Take, for instance, the granulomata—those formed by known organisms such as tubercle bacilli and the *Spirochæte pallida* can usually be reported on clearly enough, but when one comes to deal with the healing lesion or a scar showing none of the features of the known granulomata, no proper ætiological diagnosis can be given; the problem then may be clinically soluble by an enquiry into the previous history of the patient guided by such suggestions as may appear probable from the anatomical appearances. Gummata in the healing stages are notoriously difficult,

and should always be confirmed either by a search for spirochætes, or a Wassermann reaction, or by both. Sarcomata, again, are often mistaken even by fairly skilled workers; especially are they difficult in lymphatic tissues.

Let us now turn to another aspect of morbid anatomy, namely, the part it may be expected to play in the advancement of knowledge. The subject may be looked upon as a branch of anatomy, a science mainly descriptive and a part of that great group of sciences dealing with observation which may be termed natural history. Though the main naked-eye features of most disease processes are known and have been described, it cannot be said that they have been fully worked out; least of all can it be said to be so in respect of their histology. When it is recognised that the chemical processes in the normal cell as revealed by special histological technique are known only in the most fragmentary manner, it applies much more strongly to diseased tissues. The fact is the morbid anatomist has the power, subject to the limitations of the microscope and the technique employed, to see right into the centre and origin of the diseased processes. An important item in the proof of the cause of an infective process being due to a particular organism lies in the discovery by the microscope of the organisms in the site of the lesions, e.g., tubercle bacilli, and *Spirochæte pallida*. In this respect morbid anatomy and bacteriology must go hand in hand, the first controlling the findings of the second. Morbid anatomical investigations, indeed, require constant confirmation and control by bacteriological and experimental methods. Morbid anatomy without bacteriological and experimental controls reverts to a purely anatomical and descriptive science. On the other hand, bacteriology, if applied to medicine without the controlling guidance of morbid anatomy, tends to become botanical. When these subjects can be prosecuted in sympathy, the one acts as a stimulant to the other.

An aspect of morbid anatomy which offers ample scope for investigation in conjunction with clinical work is the effect in the living of lesions of organs and particular parts of organs. Much progress has already been made, as, for instance, in the manifestation of lesions of the suprarenal, thyroid, and of such viscera as are liable to destructive phenomena. Such investigation has been perfected in a high degree in the central nervous system, but with some notable

exceptions the same can hardly be said of lesions of the cardio-vascular system; despite all the energy that has been spent upon it, we have still to seek for anatomical evidence in certain cases of cardiac failure. The right method for such cases is that pursued by Mackenzie, who, after observing clinical symptoms in his patients for prolonged periods with the accuracy of a skilled observer, endeavoured to elucidate these symptoms in the light of the anatomical appearances after death. These are problems in which the general practitioner can do most useful work if he is given the opportunity by being associated with an active department of morbid anatomy. An intelligent patient suffering from an obscure and doubtful disease, and in sympathy with his doctor, seldom fails to appreciate the difficulties of medical practice. These are the cases which, if carefully recorded during life, and examined post-mortem, will of a certainty add to the knowledge of medicine. The consent of many such patients can be obtained readily enough to a post-mortem examination. If this method were pursued as opportunity offered, the accuracy of clinical methods would be enhanced and the science of medicine would be subject to a constant revision.

It may confidently be hoped that as the disturbing conditions aroused by the war settle down, research will be stimulated, and teaching in medicine will be subject to revision. Though morbid anatomy deals with the dead, there is no reason why in both respects of research and teaching it should not be made a living subject. One aspect of it deals undoubtedly with dry bones and pickled specimens in bottles, but the processes which these specimens reveal are those in the living bodies of patients in the wards to which they can constantly be referred. Some experience in the teaching of students on these lines has convinced me that it is the right and only method. The keenness or apathy of the student ought to be a guide to the teacher of the real value of his teaching, and under this method when morbid anatomy consists not in the identification of lesions of dead specimens, but in the recognition of a process which can be identified in the living, his keenness shows no tendency to wane. It is these thoughts that stimulate the main plea of this paper for a full recognition of the value of morbid anatomical teaching, and for a thorough reorganisation of departments of morbid anatomy in relation to schools of medicine.

LEUCOCYTES AND PROTOZOA

By E. S. Goodrich and H. L. M. Pixell Goodrich, Oxford

INSTANCES of Protozoa known to be destroyed by leucocytes are decidedly rare, whereas, in animals infected with bacteria one may expect to find some phagocytosis taking place, however susceptible the host may be. Bacteria taken up by leucocytes never multiply, and generally degenerate rapidly, although they may retain their virulence for a time, even occasionally surviving their host cells. However, they have not the power possessed by protozoa, such as Leishmania, Toxoplasma, certain Leucocytozoa and Hæmogregarines, of adapting themselves to passing through important stages of their life-history in such positions. Some of these protozoa seek out phagocytes as their host cells, wherein they multiply, and soon cause degenerative changes, first made apparent by a necrosis of the nuclei. Many other protozoa live free in the fluids of the body immune under ordinary circumstances to the attack of leucocytes.[1] Among blood parasites are the well-known Trypanosomes and Trypanoplasms, also certain intestinal flagellates such as Giardia, Trichomonas, Trichomastix (8) and Leptomonas (28), sometimes found in the blood of reptiles. These intestinal flagellates are perhaps the most striking examples, for since they cannot be regarded as true blood parasites, one would expect them to be rapidly destroyed. Other protozoa, such as many Coccidia and Myxosporidia, live in the tissues of the body, especially in the connective tissues and muscles. These parasites, though for the most part motionless and constantly exposed to wandering phagocytes, are not known to be interfered with by them. Not only may leucocytes serve as hosts to certain protozoa, they may even be used as food by some parasitic amœbæ. *Entamœba gingivalis* devours leucocytes, especially the small mononuclear corpuscles or lymphocytes brought to the site of pyorrhœa

[1] In speaking of leucocytes, it is understood that we mean leucocytes in general, not necessarily the hæmic ones, which have been proved to be only wandering through the blood as through tissues in general.

lesions, and these corpuscles may be seen in various stages of digestion, Fig. 1. The favourite habitat of this parasite is just below the tartar ridge, where it is surrounded by abundance of leucocytes in the issuing pus (39). It has also been stated that *Entamœba histolytica* sometimes engulfs leucocytes (3) as well as the more usual hæmatids.

It is impossible to attribute this impotence of leucocytes in the presence of protozoa to the size of the parasites, for we know that some Microsporidia, e.g., Thelohania, are smaller than certain bacteria and much smaller than many foreign particles which are readily phagocyted. Also, it is known how effectually the leucocytes of some Invertebrates can deal co-operatively with relatively huge Gregarines (see below). However, as far as Vertebrates are concerned, among the very few protozoa which have been shown to be devoured by the phagocytes of a susceptible animal are the malarial parasites (Hæmamœbæ). Even here there is difference of opinion as to the extent to which the phagocyte is an active enemy of the hæmamœbæ, and few pathologists can be found now to support Metchnikoff's opinion that to phagocytes alone we owe spontaneous recovery in malaria.

Not long after the discovery of the specific parasites of this disease by Laveran (24, 1880), Marchiafava, Celli, and Guarnieri are stated (30, p. 174) to have studied "the phenomena of their phagocytosis directly under the microscope in blood as it circulates." In addition, Golgi, Metchnikoff, Bignami, Osler, and other pioneer workers on malaria describe the process as taking place in the blood or organs, especially the spleen and liver. Just previous to schizogony a hæmamœba, for instance *Plasmodium vivax* of tertian malaria, almost completely fills the infected hæmatid, which then bursts, setting free a large amount of melanin and the young merozoites. The latter invade other corpuscles, and as a rule repeat this non-sexual cycle. As the setting free of a new generation of merozoites is known to synchronise with an attack of fever, and phagocytosis has been demonstrated to be most marked in the early hours of the pyrexial period—one would expect the hæmamœbæ devoured to be chiefly these minute forms without pigment. However, although parasites have been said to be ingested, we can find no mention of this particular stage. Of course dead and dying parasites

and cells as well as the melanin freed from them are rapidly seized; but this is no proof of the phagocytosis of living parasites. The presence of melanin in circulating corpuscles is one of the chief characteristics in the diagnosis of malaria, and was described even before the parasite was discovered.

Unfortunately observations as to phagocytosis of malarial parasites in lower animals are not nearly so complete as they should be—so many observers have been content to record the presence of hæmatozoa without studying their behaviour and fate in the organs of the body. Now since the tissues of such animals can be examined perfectly fresh at any stage of infection, interesting results should be obtained free from possibility of error.

Berenberg-Gossler, (1) after careful investigation of *Plasmodium kochi* and *P. brasilianum* in monkeys, states that he cannot confirm the generally accepted occurrence of phagocytosis of living parasites even in the spleen. In bird malaria, however, Danilewsky[2] (14) and Cardamatis (4) have described phagocytic destruction of parasites by leucocytes, and also by the large endothelial cells (macrophages) of the spleen. Labbé (22, p. 239) on the other hand, states that these parasites live voluntarily in such cells.

The leucocytes described as being phagocytic in malaria are almost entirely the large mononuclear or hyaline corpuscles, and the relative increase of these during the disease notwithstanding a marked decrease of the total number of leucocytes in the general circulation (leucocytopenia) is another argument in favour of phagocytosis being at any rate a factor in recovery, if not the sole cause of immunity in this disease.

Malaria is further interesting as being one of the few human protozoal diseases in which a certain tolerance may be established between host and parasite. This tolerance may be fairly permanent, as in many natives in malarial districts, or quite temporary, as in patients subject to frequent relapses. In these cases a few parasites remain over in the host, and it must be assumed that these have in some way become resistant to the phagocytes, antibodies, quinine, or whatever generally causes their destruction, and that it is only

[2] Most of Danilewsky's much-quoted experiments had to do with the injection of malarial blood from one animal into another. Under these conditions, the foreign corpuscles themselves are immediately devoured by phagocytes and therefore the contained parasites are also gradually digested by these cells.

by an increase of this resistance or by a lowering of the host's vitality that a relapse can be caused.

No observations have been made, so far as we can ascertain, as to phagocytosis of other parasites normally inhabiting red blood corpuscles, as for example the Piroplasms of mammals, and the genera Halteridium and Hæmoproteus of birds.

The only known instance of phagocytosis of trypanosomes is after their inoculation into naturally immune or immunised animals. The blood of the rat about ten days after infection with *Trypanosoma lewisi* may swarm with parasites—their number being as great as that of the hæmatids. Multiplication then ceases and the parasites die out, sometimes rapidly; but there is no evidence to show that they are engulfed by phagocytes. The rat is then immune against a fresh infection with this species of trypanosome, and this immunity can apparently be accounted for by the fact that the rat's phagocytes are now actively hostile to the parasites. Laveran and Mesnil (26), who have inoculated *T. lewisi* into the peritoneal cavity of an immunised rat, describe the seizing of the active trypanosomes by the cœlomic leucocytes. In districts infected with trypanosomiases the big game and some other indigenous animals have been shown to act as reservoirs of trypanosomes. The explanation of this tolerance is still obscure. Cold-blooded vertebrates are likewise known habitually to harbour trypanosomes or trypanoplasms in their blood, and, although phagocytosis seems not to have been recorded in such cases, it would appear likely that it takes place at some stage of their life history.

In spite of the leucocytes appearing to have so little direct effect in ordinary cases, yet the lethal trypanosomiases, at any rate, are essentially diseases of the lymphatic system. In sleeping sickness there is an enormous proliferation of lymphocytes, probably due to a toxin such as has been demonstrated in some trypanosomes (42). The lymphatics around all the blood vessels become crowded with these small mononuclear leucocytes which interfere with circulation to the brain, giving rise, according to Bruce (2), to the characteristic symptoms of the disease.

Before discussing further the nature of tolerance and other problems relative to the reaction of the leucocytes towards protozoa, we will mention briefly other parasites known to infect leucocytes.

Classified with hæmamœbæ among the Hæmosporidia are the closely allied Leucocytozoa. The Hæmogregarines which used to be placed with them are now known to have closer affinities with Coccidia. Certain species of both these types of hæmozoa inhabit leucocytes, while closely related forms live in red blood corpuscles. A few species, e.g., *Hæmogregarina agamæ*, may inhabit either leucocytes or hæmatids, and therefore the nature of the host cell does not seem to be of great systematic importance.

The Leucocytozoa, restricted so far as is known to birds,[3] are found in blood corpuscles which are sometimes fusiform in shape, and are so altered in appearance that it is difficult to make out whether they were originally leucocytes or hæmatids. However, as a rule, they appear to be leucocytes, as in the case of *L. lovati* (Fantham, 15) of the grouse. Léger (27) has shown that while the infected corpuscles are mononuclear leucocytes in the case of crows, which he has found so frequently parasitised in the Champagne district, in the case of *Leucocytozoa ziemanni* from the great owl the infected corpuscles are erythroblasts. These hæmatids are also shown by França (16) to be the corpuscles parasitised in the case of the blackbird and hawk.

Thus we must conclude that either kind of blood corpuscle can serve as host to various species of Leucocytozoa. Several young parasites are sometimes found in one host cell, and it is fairly common to find two adults of the same or opposite sex inhabiting the same cell, fragments of which remain round the parasites even during reproduction. They appear to do no harm except to the individual cell infected; the slender evidence published by Wickware (49) as suggestive of *L. anatis* being the cause of a fatal outbreak of disease among ducks near Ottawa has not been confirmed.

Hæmogregarines are found in the blood of all classes of vertebrates, but chiefly in those with cold blood, such as fishes and reptiles. In these latter they generally inhabit the red corpuscles, but in mammals they occur more usually in leucocytes. They can be

[3] The invertebrate host is not known, but is almost sure to be one of the etoparasites (fleas, lice, etc.) infesting the birds. There evidently is a cold-blooded host, for it is only when the blood is put on a cold slide that ripe microgametes become free and active, that is, "exflagellate," as in the malarial parasites. The transmitting agent can be determined only by examining early stages of infection in nestlings. Leucocytozoa are reported to be common in some parts of England, e.g., Bournemouth (9), but we have not found them in many different kinds of birds examined in the Oxford neighbourhood.

distinguished from true Leucocytozoa since they have a different life history, for instance they do not "exflagellate." Sometimes the body of the parasite is enclosed in a distinct membrane which no doubt helps to protect it from the digestive action of its host. As a rule they have very little, if any, pathogenic effect except on the one cell parasitised. Among Hæmogregarines is included the first intracorpuscular parasite discovered, namely Drepanidium of the frog (Lankester, 1871). This harmless form has been seen to be devoured by phagocytes (22), and so has the more destructive Karyolysus of lizards. *Hæmogregarina muris*, which occurs as a harmless parasite in the leucocytes of wild rats, has been described by Miller (33) as causing lethal epidemics among tame white rats. This is, however, an intracellular parasite of the liver, but after schizogony the merozoites pass into the capillaries and are taken up by the leucocytes, where they increase in size and make themselves generally at home until such time as they may be taken up by the invertebrate host (rat mite).

The other Protozoa inhabiting leucocytes are the various species of Leishmania and Toxoplasma. Since the latter genus has been shown by Splendore (48) to develop a flagellated stage in cultures, as was proved first by Rogers for Leishmania, both these genera may be included among Flagellates and be considered together. The parasites as found in the vertebrate host are small oval or rounded bodies multiplying by fission and generally inhabiting mononuclear leucocytes, Fig. 2, or large endothelial cells, Fig. 3; but occasionally they are found in polymorphonuclear leucocytes.

According to Laveran (25) the genus Leishmania contains two species only: *L. donovani*, the cause of visceral leishmaniasis, and *L. tropica*, giving rise to cutaneous leishmaniasis, including the well-known Tropical Sore (*Bouton d'orient*) of the Mediterranean regions, and the various forms of American leishmaniasis.

Visceral leishmaniasis in India takes the form of the deadly disease commonly known as Kala Azar; the milder Mediterranean form generally occurs in children or dogs.

Toxoplasma has now been recorded from several animals (37), but the original and best-known species is *T. gondii*, recorded by Nicolle and Manceaux from the gondi of Tunisia.

The symptoms of both visceral leishmaniasis and toxoplasmiasis

EXPLANATION OF ILLUSTRATION

The Figures were drawn with a camera lucida at a magnification of 1600, except Fig. 7, which is magnified only 600 times.

Fig. 1. *Entamœba gingivalis*, containing leucocytes undergoing digestion. *n*, nucleus of Entamœba; *nl*, nucleus of half digested leucocyte; *np*, nucleus of polymorphonuclear leucocyte.
Ehrlich's Hæm. and Orange G.

Fig. 2. Mononuclear leucocyte of a mouse containing several Toxoplasma t. The nucleus of the leucocyte, which is degenerating.
Iron Hæmatoxylin and Licht Grün.

Fig. 3. Endothelial cell of a mouse containing numerous Toxoplasma t., actively dividing. Note the hypertrophied and necrotic nucleus of the host cell, *nb*.
Iron Hæmatoxylin and Licht Grün.

Fig. 4. Section of a "Plasmodium" of Myxocystis from the sperm sac of *Tubifex rivulorum*, showing covering of fine processes, vegetative nuclei, *n*, and spores, *sp*.
Iron Hæmatoxylin and Pieronigrosin.

Fig. 5. Blood of *Carcinus mænas*, equal portions of two preparations: a, Normal Blood showing 4 leucocytes, *l*.
Iron Hæmatoxylin and Orange G.
b, Infected with Thelohania, showing young trophozoites, *p*, with spherical nuclei and no leucocytes.
Giemsa.

Fig. 6. Leucocyte of *Arenicola ecandata*, living.

Fig. 7. Section through a cyst containing a pair of associated trophozoites of *Gonospora arenicolæ*, *p*, undergoing degeneration, and showing the accumulation of leucocytes, *l*, outside the cyst, *c*.
Iron Hæmatoxylin and Picrorosine.

Fig. 8. A small portion of a cyst similar to that shown in Fig. 7, more highly magnified. *p*, Gonospora degenerating; *l*, leucocyte.

Fig. 9. Leucocyte of Lumbricus, living, *pr*, membranous process.

Fig. 10. Leucocyte of Lumbricus, fixed in Iodine to show the expanded membranous processes, *pr*.

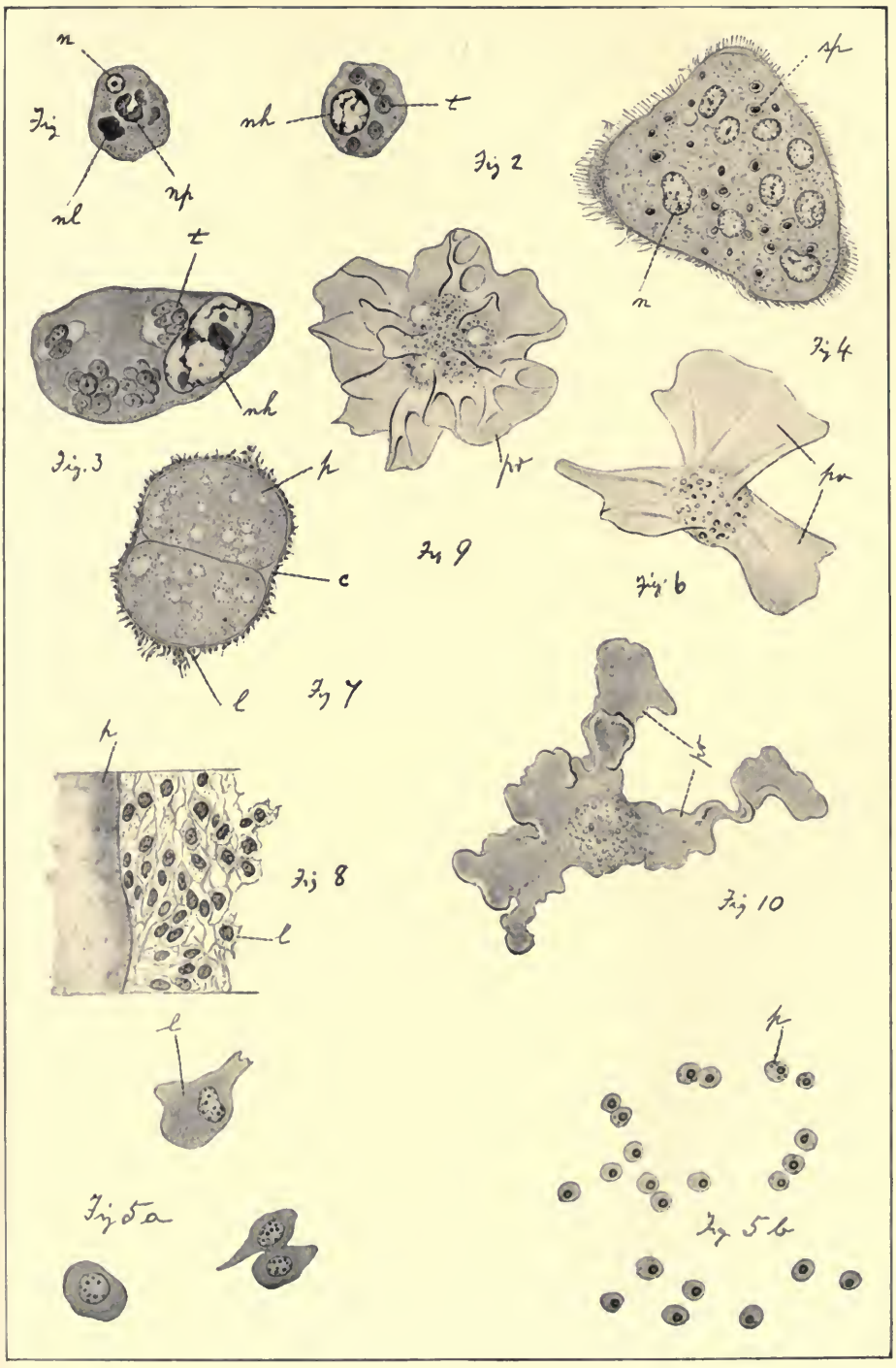

Fig 1

Fig 2

Fig 3

Fig 4

Fig 5a

Fig 5b

Fig 6

Fig 7

Fig 8

Fig 9

Fig 10

include hypertrophy of the spleen, in which organ parasites may be found often when absent from the peripheral blood. This splenomegaly is accompanied by more or less fever and a marked leucocytopenia. The colourless corpuscles, one of which is normally present to about 625 red, may disappear until there is only 1 to 2000 or more hæmatids. Notwithstanding this, there is in leishmaniases, as also in malaria and trypanosomiases, a marked increase of large mononuclear corpuscles relative to polymorphonuclear. In fact this condition appears to be characteristic of protozoal diseases as distinct from bacterial, in which the polymorphonuclear leucocytes are in somewhat greater excess than normally. In protozoal diseases also the leucocytopenia appears to be lasting, not merely transient as in pyogenic (45) and some other bacterial infections (44), where the leucocytes only appear to collect temporarily in the blood vessels of the viscera, especially the lungs, liver, and spleen, and soon reappear in the peripheral circulation. In fact the behaviour of many protozoa suggests that they are able to secrete a leucocytotoxin, and this has already been shown to be the case in the blood of leishmaniasis patients (29).

We pass now to the consideration of Invertebrates, whose leucocytes correspond roughly to those of Vertebrates in behaviour, variety of form and in the staining property of their granules—see Kollman (21). The first fact to strike one is that in the Invertebrata no Protozoa have been shown to inhabit an unchanged leucocyte. Mrazek (34) certainly claims that the relatively huge masses floating in the cœlomic fluid of some aquatic Oligochætes, e.g., Tubifex and Limnodrilus, and originally said to be the plasmodia of Myxocystis with thousands of spores, are in reality greatly hypertrophied leucocytes containing thousands of Microsporidia. This point requires further investigation, and if true in the case of Myxocystis will probably also prove to be true with *Dubosquia legeri* (36*a*), parasitic in the white ant. A section of this floating mass, with its covering of fine cilia-like processes and the developing spores of Myxocystis contained in it, is figured from the sperm-sac of Tubifex (Fig. 4).

These rather rare parasites belong to the little understood Microsporidia, and there is always difficulty in obtaining hosts with sufficiently early stages to determine such points. As a rule

all the parasites reach a certain stage at almost exactly the same time. Another and better known genus of the Microsporidia is Nosema, notorious as the cause of epidemics among silkworms (pébrine due to *N. bombycis*) and among honey-bees (*N. apis*). But it does not seem definitely established that phagocytosis occurs in these insects, which have few and relatively inactive leucocytes. Metchnikoff (31), however, states that the spores of Microsporidia are to a slight extent attacked in Daphnia.

In many cases, far from being able to deal with such parasites as Microsporidia, the leucocytes seem to disappear from the blood when infected. Pérez (1904) has recorded this fact in a crab (*Carcinus mænas*) infected with *Thelohania mænadis;* and in a specimen from Plymouth, which was found and passed on to us by the late Capt. Geoffrey Smith, the blood was swarming with minute trophozoites of this parasite (Figs. *5a* and *b*). Apparently in consequence of this hardly a leucocyte could be found in the blood, which had also lost its power of coagulation, so that the crab gradually bled to death on having a portion of one of its appendages removed. Of course it is possible that the leucocytes had taken refuge in one of the lymphoid glands; it would be interesting to examine these, and also to test the blood for a leucocytotoxin. Unfortunately we have not succeeded in obtaining further infected specimens; they appear to be rare at Plymouth and in the Solent, where we have examined over a hundred crabs without finding any.

Passing to the true Sporozoa, we find various families of Gregarines living in the body-cavities of Annelids, Insects, and Echinoderms. In each group the parasite is sooner or later drastically dealt with by the leucocytes of the host. The struggle between Monocystis and the phagocytes of the Earthworm is one of the historic cases dealt with by Metchnikoff (31). Another instance is found in the marine polychæte, *Arenicola ecaudata*, the cœlom of which is generally infested with a large Gregarine, *Gonospora arenicolæ*, often seen in large numbers and in various stages of development. It is from the spores hatched in the alimentary canal that the young gregarine or sporozoite penetrates the wall of the intestine and eventually passes into the cœlom. Here it generally becomes secondarily attached by means of an

elongated epimerite to the body-wall or nephridial cœlomostome. Thousands of such parasites (trophozoites) may be found in the cœlom growing to quite a large size, and apparently ignored by the host. Having completed their growth such trophozoites normally associate in pairs, and secrete round themselves a cyst which may be as much as 2 mm. in diameter. At this stage, indeed, as soon as the protoplasm ceases its violent streaming movements, the parasites are vigorously attacked by the host's leucocytes, which are extraordinarily active. Unable to deal singly with such a large body as the cyst, they co-operate, spreading over its surface until the cyst is enclosed in a film composed of flattened leucocytes. Layer upon layer of these cells may be added (Figs. 6 and 7), and cysts thus smothered in a thick coat can be found in all stages of degeneration. Some seem to succeed in completing their reproduction and form normal spores; but generally the associates begin to degenerate at an early state, and their protoplasm becoming vacuolated they finally disintegrate. Many cysts containing spores suffer the same fate.

Such is the behaviour of the leucocytes towards parasitic Gregarines in several polychæte worms, as described in the works of Siedlecki (47) and Caullery and Mesnil (5), while Cuénot (12) has given a similar account of the fate of a gregarine in the insect Gryllus. In the echinoderms Spatangus and Echinocardium the gregarines Urospora and Lithocystis are likewise attacked by leucocytes in large numbers (38). This strange capacity of the leucocytes of the Invertebrates with large vascular or cœlomic spaces to co-operate for defence against an intruding parasite is most remarkable. It has long been known that in these animals the leucocytes have a tendency to join to form so-called "plasmodia" described by Geddes in the Sea Urchin (17). The apparent clotting of the blood is due in most Invertebrates merely to the coalescence of the leucocytes in irregular masses and strands. Now this property of "plasmodium" formation appears to be due to the peculiar character of the "pseudopodia" of the leucocytes, which are not outstanding finger-shaped or spine-like processes, as generally depicted, but delicate membranous folds thrown out in various directions, as described by one of us in the worm Glycera in 1898 (18), and further dealt with in a forthcoming paper.

These spreading membranes may be rapidly extended or withdrawn, and when coming into contact with some foreign object quickly spread over its surface as a thin film of protoplasm. They are especially well-developed in Annelids (Figs. 6 and 9) and Echinoderms; and that they are not artifacts, but are present on the normal corpuscles floating in the fluids of the body, may be proved by dropping the fluid into a dilute watery solution of iodine, when the membranes will be found fixed in an expanded condition (Fig. 10). It is by the ready junction of these processes that the coalescence of the leucocytes takes place to form the "plasmodia" which so quickly surround the cysts of parasitic protozoa; but, as Michel maintained (32), the cells in these coalesced masses do not really lose their individuality, and may on occasion regain their independence.

Although there are few records of Protozoa being submitted to phagocytosis, in many cases they have not been studied from this point of view. There are several Ciliates which occur in the body cavities of Invertebrates, for example, Annelids (46, 20), Crustacea (7), Sagitta (19), Strongylocentrotus (38), but there are no records of their being destroyed by phagocytes, except in the case of the common earthworm, where Keng (20) states that these parasites on becoming quiescent are surrounded by leucocytes and may sometimes be seen contained in a large vacuole of a phagocyte. In most cases, observations are needed as to the life histories of these Ciliates and especially as to their ultimate fate. During their actively moving stage they are apparently, as one would expect, quite free from molestation by leucocytes.

From the review of the subject given above it is obvious that much research is still necessary before reaching definite results. Nevertheless we may attempt to indicate provisional conclusions that may be drawn with regard to mutual reactions between leucocytes and protozoa in animals.

As regards phagocytosis Metchnikoff supposed that protozoa warded off the attack of leucocytes by their active movements. This explanation is, however, insufficient, for many motionless forms are just as free from attack as are the tissues themselves or the genital products floating in the cœlom. However, just as the ova and spermatozoa in such cases may be attacked under certain

conditions (43, 6) so it is with the parasites. It must also be remembered that all the sporozoa pass a certain stage of their life history actually in the cells of the host, and that many of them, like the Coccidia, continue to live in the tissues quite unharmed by leucocytes. Some would attribute this immunity from attack to the leucocytes being merely indifferent to the protozoa. This explanation, however, is not satisfactory, since it is well known that the most inactive substances, such as carbon or glass, are rapidly ingested by phagocytes. We must then conclude that these protozoal parasites are avoided by the leucocytes owing to the secretion of some substance which renders them negatively chemiotactic.

Further we may conclude that the defences against invading organisms are far better developed in Vertebrates than in Invertebrates. No case seems yet to have been discovered in a Vertebrate of a bacterium living habitually in the fluids of the body, in other words, no bacterium has succeeded in establishing a condition of tolerance either in the cœlom or in the blood vascular system. This failure of the bacteria is due either to the phagocytic action of the leucocytes, or to the secretion of efficient bactericidal substances. On the other hand, in the Invertebrates cases are known of the habitual presence of bacteria in the cœlomic fluid; as for instance in the common earthworm (20); and certain protozoa have succeeded in thus establishing themselves in Vertebrates as well as Invertebrates.

Such constant parasites are said to be tolerated by the host. Since the parasites are characteristically capable of reproducing in enormous numbers, tolerance can only be explained as due to a balance having been established between their reproductive powers and the destructive powers of the host. It is obvious that such a state cannot be permanent—sooner or later the balance must be upset, perhaps owing to some change in external conditions, and either host or parasite will gain the upper hand. Tolerance then is only a stage between disease and immunity. The total absence, for instance, of cœlomic Gregarines from *Arenicola grubei* and their constant presence in *A. ecaudata*, when both these species live together in the sand under identical conditions, is probably to be explained as due to *A. grubei* having passed through the stage of tolerance to that of immunity. The same explanation probably

applies to similar phenomena among other groups of animals which at first sight appear so mysterious.

It is by no means yet certain whether "protozoocidal" substances are really secreted by the host, though it seems to be clear, on the other hand, that in some cases protozoa secrete toxins. The protozoa, perhaps owing to their relatively high organisation, are more capable of resisting the attacks of their host than bacteria. At the same time, owing to their complicated life histories, it is often necessary for protozoa to reach another host before further multiplication can take place, and therefore they are effectually prevented from overcrowding and killing their host. The combination of these factors in the case of protozoa must help considerably towards the establishment of tolerance.

BIBLIOGRAPHY

1. Berenberg-Gossler, H. von, "Malaria Plasmodien," Arch. f. Protistenk., 1909, XVI, p. 245.
2. Bruce, D., Trypanosomiasis," Osler's "Modern Medicine," 1907, I, 460.
3. Brug, S. L., "Pigment und andere Einschüsse in Dysenterieamöben," *Arch. f. Schiffs- u. Tropen-Hyg.*, 1916, 433–436.
4. Cardamatis, J. P., "Le paludisme des oiseaux en Grèce," *Centralbl. f. Bakteriol. u. Parasitenk.*, 1^te Abt., 1909, Orig. 52, 361.
5. Caullery, M., and Mesnil, F.,"Sur une Gregarine cœlomique nouvelle," *Compt. rend. Acad. d. Sc.*, 1898, CXXVI, 262.
6. Caullery and Siedlecki, M., "Sur le résorption phagocytaire des produits génitaux inutilisés chez Echinocardium cordatum," *Compt. rend. Acad. d. Sc.*, Par., 1903.
7. Cépède, C., "Infusiores astomes," *Arch. de zool. expér.*, 1910, III, 341–609.
8. Chatton, E., "Présence d'un flagellé intestinal du genre Trichomastix dans le sang et les organes du gecko," *Compt. rend. Soc. de Biol.*, 1919, LXXXI, 343.
9. Coles, A. C., "Blood Parasites found in Mammals, Birds and Fishes in England," *Parasitology*, 1914, VII, 17–61.
10. Craig, C. F., "Malarial Fevers," 1909.
11. Cuénot, L., "Étude physiologique sur les Crustacés Decapodes," *Arch. de biol.*, 1893, XIII, 245.
12. Cuénot, L., "Étude physiologique sur les Orthoptères," *Arch. de biol.*, 1895, XIV, 293.

13. Cuénot, L., "Recherches sur l'évolution et la conjugaison des Gregarines," *Arch. de biol.*, 1901, XVII.
14. Danilewsky, "Contrib. à l'étude des phagocytes," *Ann. de l'Inst. Pasteur*, 1890, IV, 432.
15. Fantham, F. B., "Parasitic Protozoa of the Red Grouse," *Proc. Zool. Soc.*, 1910, 692.
16. França, C., "Quelques Observations sur le genre Leucocytozoon," *Bull. Soc. path. exot.*, 1915, VIII, 229–241.
17. Geddes, P., "On the Coalescence of Amœboid Cells into Plasmodia and in the So-called Coagulation of Invertebrata Fluids," *Proc. Roy. Soc. Lond.*, 1880, XXX.
18. Goodrich, E. S., "Nephridia of Polychæta, II," *Quart. J. Micr. Sc.*, 1898, XLI, 439.
19. Ikeda, Iwaji, "A New Astomatous Ciliate in the Cœlome of Sagitta," *Annot. zool. japon.*, 1917, IX, 317.
20. Keng, Lim Boon, "On the Cœlomic Fluid of Lumbricus Terrestris, in Reference to a Protective Mechanism," *Trans. Roy. Soc.*, 1895, 186.
21. Kollman, Max, "Recherches sur les Leucocytes et le tissue lymphoide des Invertébrés," Paris, Masson et Cie., 1908.
22. Labbé, A., "Parasites Endoglobulaires," *Arch. zool. expér.*, 3d ser., 1894, II, 55.
23. Lankester, E. R., "On Undulina, the Type of a New Group of Infusoria," *Quart. J. Micr. Sc.*, 1871, 387.
24. Laveran, A., "Note sur un nouveau parasite," *Bull. Acad. de méd.*, Paris, Nov., 1880.
25. Laveran, A., "Leishmanioses, Kala-Azar, Bouton d'Orient, Leishmaniose américaine," Paris, Masson et Cie., 1917.
26. Laveran, A., and Mesnil, F., "Trypanosomes and Trypanosomiases," Masson, Paris, 1912.
27. Léger, M., "Observations sur quelques Leucocytozoon d'Oiseaux de la région de Reims," *Bull. Soc. path. exot.*, 1917, X, 28–33.
28. Léger, M., "Infection sanguine par Leptomonas chez un saurien," *Compt. rend. Soc. de Biol.*, 1918, LXXXI, 772.
29. Maggiore, S., and Sindoni, M., "Sulla presenza di leucotossine circolanti nel siero di sangue di infermi di leichmaniosi interna," *Pediatria*, 1917, 25, 81–88. *T. D. Bull.*, 1917, X, 2, 66.
30. Marchiafava, E., and Bignami, A., "Malarial Fevers," Transl. London, 1894.
31. Metchnikoff, E., "L'Inflammation," Paris, Masson, 1892.
32. Michel, "Sur la prétendue fusion des cellules lymphatiques en plasmodes," *Compt. rend. Acad. de Sc.*, CVI, 1888.

33. Miller, W. W., "Hepatozoon perniciosum," *Hygienic Laboratory Bull.*, 46, 1908.
34. Mrazak, A., "Zur Auffassung der Myxocystiden," *Arch. f. Protistenk.*, 1910, XVIII, 245.
35. Osler, W., "Malarial Fever," "Allbutt's System of Med.," II, 1897.
36. Pérez, Ch., "Microsporidies Parasites des Crabes d'Arcachon," *Bull. Stat. Biol. d'Arcachon*, 1904–5, 1–22.
36a. Pérez, Ch., Duboscqia legeri, *C. Rend. Soc. Biol.*, 1908, LXV, 631.
37. Pixell H. L. M., "Toxoplasma gondii," *Proc. Roy. Soc. B.*, 1913, LXXXVII, 67.
38. Pixell Goodrich, H. L. M., "Sporozoa of Spatangoids," *Quart. J. Micr. Sc.*, 1915, LXI, 81.
39. Pixell Goodrich, H. L. M., and Moseley, M., "On certain Parasites of the Mouth in Cases of Pyorrhœa," *J. Roy. Micr. Soc.*, 1916, 513–527.
40. Rogers, L., "Trypanosomes from the Spleen. Protozoic Parasites of Cachexial Fevers and Kala-Azar," *Quart. J. Micr. Sc.*, 1904, XLVIII, 367.
41. Rogers, L., "Chronic Splenomegaly in Lower Bengal with Special Reference to the Prevalence and Clinical Differentiation of Kala-Azar," *Indian M. Gaz.*, 1917, LII, 7–15.
42. Schilling, C., and Rondoni, P., "Ueber Trypanosomen-Toxine und Immunität." *Ztschr. f. Immunitätsforsch. u. exper. Therap.*, 1913, XVIII, 491. Synopsis by Mesnil, *Bull. Inst. Past.*, 1914, XII, 137.
43. Schneider, A., "Ueber die Aufloesung der Eier und Spermatozoen in dem Geschlectsorgan," *Zool. Anz.*, 1880, III.
44. Sellards, A. W., and Baetjer, W. A., "The Clinical Significance of the Irregular Distribution of Cells and Parasites in the Blood," etc., *Johns Hopkins Hosp. Bull.*, 1918, XXIX, 328.
45. Sherrington, C. S., "On Changes in the Blood Consequent upon Inflammations of Acute Local Character," *Proc. Roy. Soc.*, 1894, LV, 161.
46. Siedlecki, M., "Herpetophrya astoma, infusoire cœlomique des Polymnies," *Bull. Internat. Acad. sc. de Cracovie*, 1902.
47. Siedlecki, M., "Quelques Observations sur le rôle des Amibœtes," *Ann. de l'Inst. Pasteur*, 1903, XVII, 449.
48. Splendore, A., "Des Formes flagellées et des Gamétes dans le Toxoplasma cuniculi," *Bull. Soc. path. exot.*, 1913, VI, 318.
49. Wickware, A. B., "Is Leucocytozoon Anatis the Cause of a New Disease in Ducks?" *Parasitology*, 1915, VIII, 17.

FURTHER OBSERVATIONS ON THE EFFECTS OF ROENTGENIZATION AND SPLENECTOMY ON ANTIBODY PRODUCTION

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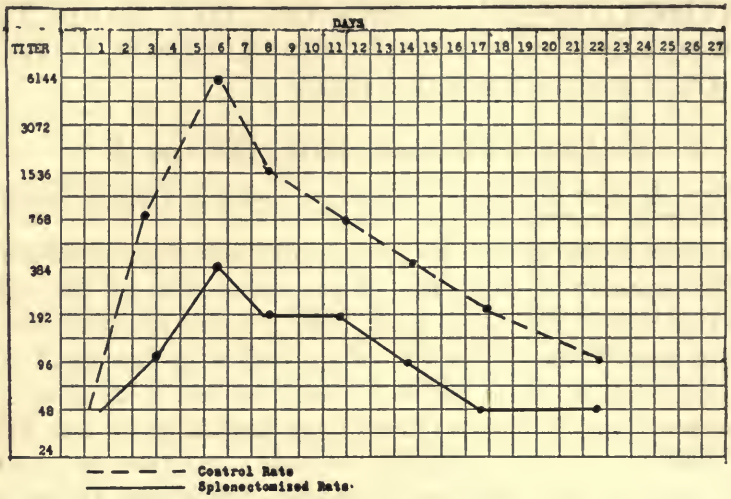
In previous papers (1) I have recorded observations which show that exposure of white rats, dogs, and rabbits to the roentgen ray at about the same time that antigen is introduced may restrain greatly the production of antibodies as measured by the antibody content of the serum. I have also noted (2) that in dogs splenectomy just before the injection of foreign blood was followed by a lower but otherwise typical antibody curve than is usually the case in dogs under otherwise comparable conditions. In the meantime additional observations have been made on roentgenization and splenectomy under more diversified conditions, the results of which seem to merit a brief report.

Splenectomy. Experiments on white rats gave results similar to those in dogs. Without exception the amount of lysin for sheep corpuscles was much less in the rats in which the spleen was removed at the same time that the blood was injected. As seen on Chart I the lysin curves present the same general outlines, but in the splenectomized series the latent period is longer, the height and duration less than in the controls.

Rats weighing from 70 to 80 grams were used; 1 c.c. of a 10 per cent suspension of sheep blood per kilo of weight was injected intramuscularly immediately after the splenectomy. The curves (Chart I) are composite curves based on the titers of two rats killed on each day indicated, it being practically impossible to bleed the same rat many times. The control curve gives the titer of rats of the same age and size, treated in the same way, but not splenectomized. The titer gives the highest dilution of the serum that caused distinct lysis in a mixture of 0.6 c.c. consisting of 0.2 c.c. of a 5 per cent suspension of sheep corpuscles, well washed, 0.0125 c.c. of guinea pig serum, and the indicated amount of

heated rat serum, the rest being salt solution. The tubes were incubated for two hours and then placed in the ice-box until the next morning.

CHART I. LYSIN IN NORMAL AND SPLENECTOMIZED RATS



In rabbits splenectomy from one to six days before the intraperitoneal injection of 25 c.c. of sheep blood as a rule did not interfere with the production of lysin and precipitin; exceptionally, however, splenectomy shortly before the injection seemed to suspend completely the advent of antibodies into the blood (Table I).

TABLE I.—ANTIBODY PRODUCTION IN RABBITS INJECTED WITH SHEEP BLOOD BEFORE SPLENECTOMY

Days after Injection of Antigen	Splenectomy Three Days before Injection of Antigen		Splenectomy Three Days before Injection of Antigen		Splenectomy Six Days before Injection of Antigen		Splenectomy Nine Weeks before Injection of Antigen	
	Lysin	Precipitin	Lysin	Precipitin	Lysin	Precipitin	Lysin	Precipitin
4	0	0	3072	100	192	0	3072	0
6	384	0	3072	2400	768	1600	12288	200
9	48	0	12288	4800	1536	6400	24576	3200
11	0	0	12288	6400	3072	6400	24576	6400
14	96	0	12288	12800	6144	12800	24576	12800
16	0	0	6144	25600	6144	12800	12288	12800
19	24	0	6144	25600	6144	12800	6144	6400
21	0	0	3072	25600	6144	12800	6144	3200
24	0	0	3072	19200	6144	12800		

Of six rabbits splenectomized five to nine weeks before the injection all save one developed about the usual amount of lysin and also precipitin in fairly high degree, though with a somewhat prolonged latency (Table I). Of ten rabbits, all young and healthy, splenectomized from five to nine weeks before the intraperitoneal injection of 30 c.c. of human blood, all but one failed to develop more than a trace of precipitin, but in all agglutinin of considerable strength developed as well as smaller amounts of lysin (Table II). This last result is of interest because it indicates that under certain conditions splenectomy even some time before immunization may restrain the formation of one kind of antibody more than others.

TABLE II.—ANTIBODY PRODUCTION IN RABBITS INJECTED WITH HUMAN BLOOD NINE AND SIX WEEKS AFTER SPLENECTOMY

DAYS AFTER INJECTION OF ANTIGEN	SPLENECTOMY NINE WEEKS BEFORE INJECTION OF ANTIGEN			SPLENECTOMY SIX WEEKS BEFORE INJECTION OF ANTIGEN		
	Lysin	Agglutinin	Precipitin	Lysin	Agglutinin	Precipitin
4	0	96	0	0	96	0
6	0	192	0	0	384	0
9	96	3072	0	0	3072	0
11	192	6144	0	384	6144	1600
14	384	3072	0	384	3072	1600
16	192	3072	200	384	1536	0
19	192	1536	0	192	768	0
21	96	192	0	192	768	0
26	96	192	0	96	192	0

In the experiments 25 c.c. of sheep or human blood were injected intraperitoneally in one dose. The figures in the tables give the highest active dilution of the serum in the case of the lysin and agglutinin tests, and the highest dilution of sheep or human blood in which the rabbit serum caused precipitate by the ring or contact method after two hours at the room temperature in case of the precipitin tests. The lysin and agglutinin tests were carried out in mixtures of 0.6 c.c. containing 0.2 c.c. of a 5 per cent suspension of washed corpuscles, heated rabbit serum, and in the lysin tests guinea pig serum (complement), the rest being salt solution. The complement dose was .006 c.c. in the tests for lysin for sheep corpuscles, and .02 c.c. in the tests for lysin for human corpuscles. All lysin and agglutinin mixtures were incubated for two hours and then placed in the ice box until the next morning.

Taken as a whole my results correspond well enough with those of earlier observers, some of whom obtained inhibition of antibody production from splenectomy (London (3), Deutsch (4), while others failed (Jakuschewitsch (5), Kraus and Schiffmann (6), McGowan (7)), but minute comparisons are not worth while because of great differences in the experiments, e.g., mode of injection of antigen, measurements of antibodies, etc.

Splenectomy and Roentgenization. Table III gives details of an experiment on young dogs of the same litter in which roentgenization and splenectomy, alone and combined, greatly reduced the output of lysin after injection of goat blood. The small number of dogs represented precludes any conclusion as to which procedure may be most effective, but the results of splenectomy alone or combined with roentgen ray shortly before the antigen was injected seem the more striking.

TABLE III.—ROENTGEN RAY (45 KIENBACH UNITS) AND SPLENECTOMY, SINGLY AND COMBINED, SHORTLY BEFORE AND FIVE DAYS AFTER INJECTION OF GOAT BLOOD IN DOGS

Days after injection of goat blood	1 Roentgen ray two days before antigen	2 Roentgen ray two days before injection and splenectomy five days after	3 and 4 Roentgen ray two days and splenectomy one day before injection		5 Splenectomy one day before injection	6 Splenectomy one day before and roentgen ray five days after injection	7 Control
2	0	0	0	0	0	0	48
3	0	0	0	0	48	48	192
4	0	0	0	0	96	48	348
5	96	96	48	0	0	192	768
6	384	96	48	0	0	384	1536
7	384	192	48	48	96	384	3072
8	768	384	96	48	0	384	3072
9	768	384	96	48	0	384	3072
10							
11	192	96	48	48	192	192	1536
12	192	96	48	48	0	192	768
13	192	96	48	48	0	192	384
14							
15	96	0	0	0	0	48	192
16							
17	96	0	0	0	0	96	192
18	96	0	0	0	0	48	192

In this as well as the other experiments now discussed the roentgenization was done in the Presbyterian Hospital by Earl Ball. The Coolidge tube was used, the focal distance was 8 inches, the current 5 to 6 milliamperes, spark-gap 8 inches. In the tables the dose is expressed in calculated Kienbach units. Usually two exposures were given, a major and one-fourth as long the next day.

TABLE IV.—ROENTGEN RAY (45 KIENBACH UNITS) AND SPLENECTOMY, SINGLY OR COMBINED, IN DOGS AT OR NEAR HEIGHT OF PRODUCTION OF LYSIN FOR GOAT CORPUSCLES

DAYS AFTER INJECTION OF GOAT BLOOD	1 ROENTGEN RAY ON SIXTH DAY	2 SPLENECTOMY ON SIXTH DAY	3 AND 4 SPLENECTOMY ON SIXTH DAY AND ROENTGEN RAY ON SEVENTH DAY		5 CONTROL
3					
4	192	192			96
5	768	768	192	768	384
6	768	768	384	1536	768
7	1536	1536	768	3072	768
8	3072	1536	1152	1536	1536
9	3072	3072	1152	1536	1536
10	6144	3072	1536	1536	1536
11	3072	3072	1536	1536	1536
12	3072	3072	768	1536	3072
13	1536	768	768	768	768
14	1536	768	768	768	768
15	1536		384	768	
16	1536	768	384	768	768
17			384	768	
18	1536	768			768
19			192	384	
20	768	384			384
21			192	192	
22					
23			192	192	384
24	768	384			
25					
26			192	192	192
27					
28	768	192			192

Roentgenization and Splenectomy at Height of Antibody Production. Tables IV and V and Chart II give the results of new experiments (8) on the effect of roentgen ray and splenectomy at or near the high point of the accumulation of antibody in the blood. These results indicate that neither roentgenization, as practiced, alone or combined with splenectomy, nor splenectomy alone or combined

with roentgenization, had any appreciable influence on the course and amount of antibodies in the blood when applied several days after the introduction of the antigen. The experiments covered by Tables IV and V concern in each case young dogs of one but not the same litter.

TABLE V.—ROENTGEN RAY (45 KIENBACH UNITS) AND SPLENECTOMY, SINGLY OR COMBINED, IN DOGS AT OR NEAR HEIGHT OF PRODUCTION OF AGGLUTININ FOR RAT CORPUSCLES

DAYS AFTER INJECTION OF RAT BLOOD	1 ROENTGEN RAY ON SIXTH DAY	2 SPLENECTOMY ON SIXTH DAY	3 AND 4 SPLENECTOMY ON SIXTH DAY AND ROENTGEN RAY ON SEVENTH DAY		5 CONTROL
4	96	96			96
5	192	192	0	0	192
6	192	192	192	96	192
7	384	384	192	192	384
8	768	768	384	384	768
9	768	768	768	384	768
10	768	768	768	576	768
11	384	768			384
12	384	384	768	384	384
13	384	768	384	384	384
14	192	384	384	192	384
15			384	192	
16	384	384			192
17			384	192	
18	384	384			192
19			384	192	
20	192	384			192
21			384	96	
22					
23			192	96	
24	192	384			192
25					
26			96	96	
27					
28	192	384			192

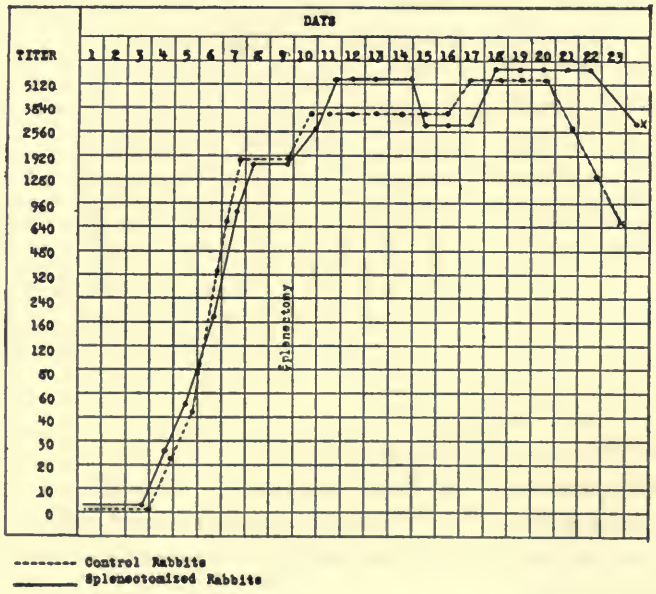
Beginning soon after splenectomy the red corpuscles were found more resistant to hypotonic solution than corpuscles of non-splenectomized animals. The increase in resistance seemed to be about the same in the splenectomized animals treated with roentgen ray as in those that were not; there was no change from the normal in the

resistance of the corpuscles of animals subjected to the ray only. In the rabbits, too, splenectomy as a rule results in an increase.

Chart II illustrates the results of a study on six healthy young rabbits, each injected with 25 c.c. sheep blood, and in two of which splenectomy was made nine and ten days later, but without any effect whatever on the precipitin titer as compared with that in the controls.

These results are in full harmony with the results obtained by London (9) in an experiment on the effect of splenectomy some

CHART II. SPLENECTOMY AT HEIGHT OF ANTIBODY CURVE



days after the production of hemolysin had started. I have reported previously that roentgenization of dogs when antibody production is well under way has little or no effect on the antibodies in the blood (10).

Roentgenization Sixteen Days before the Antigen is Introduced. Five young healthy dogs of the same litter were given each an intravenous injection of rat blood; sixteen days before three of the dogs had been exposed to roentgen ray for fifteen minutes and again for three minutes the day after (54 Kienbach units). Two days before the injection of the rat blood the leucocytes ranged from 14,666 to

17,000 in the roentgen dogs and in the two control dogs the counts were 11,333 and 15,666; the differential counts were normal. Table VI shows that the agglutinin titer ran uniformly higher in the dogs treated with the roentgen ray than in the controls.

TABLE VI.—AGGLUTININ PRODUCTION IN DOG PREVIOUSLY EXPOSED TO ROENTGEN RAY (45 KIENBACH UNITS)

DAYS AFTER INJECTION OF RAT BLOOD	ROENTGEN RAY SIXTEEN DAYS BEFORE INJECTION OF RAT BLOOD AND AGAIN FOR THREE MINUTES THE NEXT DAY			CONTROLS	
	1	2	3	1	2
3	48	24	24	96	48
4	384	192	384	96	192
5	1536	192	384	384	192
6	6144	768	1536	768	192
7	6144	768	3072	1536	384
8	3072	1536	6144	1536	384
9	6144	3072	3072	1536	768
10	3072	3076	1536	1536	1536
11	3072	3076	3072	768	1536
12	1536	1536	3072	768	384
13	1768	1536	1536	768	384
14	354	768	384	384	192
16	192	384	192	192	192
18	192	384	192	192	192
22	192	384	96	192	48
25	96	192	45	96	96

In another experiment three dogs were exposed to roentgen ray for twenty minutes (60 Kienbach units) and fifteen days later injected with goat blood. These animals developed profound effects and died a few days after the injection without having produced hardly any lysin.

The first experiment indicates that under certain conditions the roentgen ray induces such changes in the body that the power to elaborate antibodies is increased. It lies near at hand to associate this increased power with regenerative changes in the lymphatic tissues and spleen after roentgenization.

In all the experiments on dogs, the antigen, 1 c.c. of 10 per cent suspension of goat blood or rat blood per kilo of weight of dog, was injected intravenously. Only one injection was given. The figures in the tables give the highest active dilutions of the dog serums in mixtures of 0.6 c.c. containing 0.2 c.c. of a 5 per cent suspension of washed goat or rat cor-

puscles, the proper amount of dog serum, 0.0125 c.c. guinea pig serum in lysin tests, the rest being salt solution. The mixtures were incubated for two hours and kept in the ice box until the next morning.

Summary. The results recorded show that splenectomy may diminish the output of antibodies especially when practiced about the same time the antigen is injected. In the rabbit, however, splenectomy under certain conditions may have little or no effect on antibody production, as after a single large dose of sheep blood. On the other hand, even when made several weeks before injection of human blood, removal of the spleen seemed to interfere with the formation of precipitin, but further observations are needed to determine whether such selective effect occurs regularly under these circumstances.

On the whole, the effects of splenectomy at or near the time of injection of antigen appear variable and uncertain, more so, perhaps, than might be expected from the demonstrations that antibodies appear earlier in the spleen than in the blood (11), that antigen is fixed by the spleen (12), and that in the presence of antigenic substances cultures of splenic tissue outside the body may produce antibodies (13). And yet variations in results are really not surprising if we consider, first, the close relation of the spleen to the lymphatic tissues and the marrow, which are believed also to take part in the elaboration of antibodies and consequently may be capable of compensatory activities, to say nothing of the possibilities of accessory spleens; and, secondly, that the experiments of different investigators were made under diverse conditions in such important respects as kind, quantity, and mode of injection of antigen, measurement of antibody, etc. Perhaps the effects of splenectomy would not be so variable in larger series of experiments with particular effort to secure as high degree of constancy as possible of the controllable factors.

The results of several experiments indicate clearly that after antibody production is well under way, splenectomy has little or no effect on the course of the antibodies in the blood. I have noted elsewhere (14) that the usual effects of the roentgen ray and of benzene appear to be withstood when antibody production is well started. We now find that splenectomy even when reinforced with roentgenization seems subject to a similar resistance; at any rate the antibody content of the blood was not diminished markedly by

splenectomy and roentgenization at or near the height of the curve. The nature of this so-called resistance remains obscure.

It may be pointed out again that as time passes after roentgenization the power to produce antibodies may be increased, and it is suggested that this increase may be due to regenerative changes in the spleen and lymph nodes. We consequently must distinguish between the immediate and the later effects of the roentgen ray. That the ray may reduce antibody production seemed a good explanation of the increased susceptibility of guinea pigs to tuberculosis described by Morton (15); Kellert (16), however, could not confirm Morton's claim; he found that roentgenization rather increased the resistance to the tubercle bacillus at the same time as the guinea pigs seemed to become more susceptible to secondary and contaminating infections. Corper (17) also failed to produce any distinct effect on the gross tuberculous lesions in guinea pigs by a single exposure to the roentgen ray. These contradictory results invite further experiments, not only on the effect of roentgenization on antibody production, but also on phagocytosis and other cellular activities.

BIBLIOGRAPHY

1. *J. Infect. Dis.*, 1915, XVII, 415 and 1918, XXII, 28.
2. Ibid, 1909, VI, 78.
3. *Arch. d. Sc. biol.*, 1901, VIII, 328.
4. *Ann. de l'Inst. Pasteur*, 1899, XIII, 688.
5. *Ztschr. f. Hyg. u. Infectionskrankb.*, 1904, XLVII, 407.
6. *Ann. de l'Inst. Pasteur*, 1906, XX, 225.
7. *J. Path. & Bacteriol.*, 1911, XV, 262.
8. See Hektoen, *J. Infect. Dis.*, 198, XXII, p. 28.
9. *Arch., d. Sc. biol.*, 1901, VIII, p. 328.
10. *J. Infect. Dis.*, 1918, XXII, p. 28.
11. Pfeiffer and Marx, *Ztschr. f. Hyg. u. Infektionskrankb.*, 1898, XXXVII, 272. Cantacuzene, *Ann. de l'Inst. Pasteur*, 1902, XVI, 552. Tsurumi and Koda, *Ztschr. f. Immunitätsfs.*, O., 1913, XIX, 519.
12. Leuckart and Becht, *Trans. Chicago Path. Soc.*, 1911, VIII, 202.
13. Carrell and Ingebrigtsen, *J. Exper. M.*, 1912, XV, 287.
14. *J. Infect. Dis.*, 1918, XXII, 28.
15. *J. Exper. M.*, 1916, XXIV, 419.
16. *J. Med. Research*, 1918, XXXIX, 93.
17. *Am. Rev. of Tuberculosis*, 1918, II, 587.

THE IMPORTANCE OF RECORDING THE WEIGHT AT DEATH

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INDIVIDUALS die, not because they are tall or short, and not always because they are fat or thin, but, save in the case of sudden death, life usually ends with a loss in weight. Yet pathologists record with precision the exact height, but only approximately note the weight. The simplicity of the former determination and the inconvenience of the latter are the explanation for the neglect to record more accurately the more important of these two data.

A deeper significance than the mere accumulation of facts is attached to the registration of the weight. Just as the addition of cellular pathology to anatomical pathology and the later addition of bacteriology broadened the scope of the pathologist's work, the inclusion of the weight at death makes a new demand upon the pathologist, for he should explain deviations from the normal, and this leads him into the fields of chemistry and physiology.

The army hospital centers in France offered a favorable opportunity to secure body weights at death. Although the weights of the soldiers during the few weeks previous to hospital entrance were not known, their original weights at entrance into the army will become available, as well as the army tables for the average weight for the given age and height. These considerations led me to enlist the help of the pathologist, Lt. Col. David Marine, in charge of all the laboratories at the Mesves Center, and it is through his courtesy and that of his associates that the following facts are reported. It was found that the average weight at death of each man in a group of 59 men was 54 kilograms. This represented a loss from the normal weight of men of their average height and approximate age of about 15 kilograms (33 pounds)—22 per cent. This is approximately the same as Benedict found the loss of weight to be of a man who had fasted for thirty-one days. The greatest loss of any

one man was of 36 kilograms (79 pounds), or 50 per cent. Among the number there were 24 cases of broncho-pneumonia, and their average loss of weight was 14 kilograms, or 20 per cent; 12 cases of gunshot wounds with sepsis, showing an individual loss of 18 kilograms, or 27 per cent; 7 cases of tuberculosis with a loss of 20 kilograms, or 29 per cent; and 5 cases of typhoid fever whose average loss amounted to 21 kilograms, or 30 per cent.

The statistics are too meager to warrant far-reaching conclusions, but they illustrate the importance of body weights at death. For example, take pneumonia. In the lobar type we have been taught, on the one hand, by von Leyden to expect a retention of weight due to the retention of sodium chloride, a piece of work which demands confirmation, while more recently the increased excretion of nitrogen in broncho-pneumonia, found by the investigators at Camp Lee, would suggest a marked loss of weight, because each 30 grams of nitrogen lost above the intake represent the loss of 1 kilogram of muscle tissue. Is it not possible that different types of pneumonia may be accompanied by variations in the loss of weight?

The cause of the decrease in weight at death varies. Although the percentage loss of weight may be the same in fasting as in broncho-pneumonia, who would assign to it the same explanation? Obviously the loss of weight in dysentery rests upon a different basis from that which occurs in tuberculosis, but the explanation may not be as simple as first appears. It is to the pathologist in his broadened rôle that we look for the elucidation of such problems, and it is particularly appropriate that he undertake the task now when renewed attention is being devoted to studies of blood volume, which involve great changes in weight. Is the loss due to water, and is this dependent upon salt metabolism or simply to variations in the intake or outgo of water, or is it related to inroads upon the glycogen reserve or the destruction of protein and fat? How do these percentage losses compare with those which take place in fasting? The answer to these questions will foster rational therapeusis by enabling the physician to adopt specific measures for the relief of these pathological states during life.

Is it not also desirable to study the changes in weight during the early days following operation?

THE TUMOR IN SYPHILIS OF THE LIVER

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MY special interest in the subject of syphilis of the liver goes back to the days when I was a resident house officer in charge of the private wards in the Johns Hopkins Hospital. One day Sir William Osler said to me that there was a patient with an interesting abdominal tumor coming into the private ward, and asked me to examine him and make a diagnosis if I could. The patient was a very depressed individual, who promptly volunteered the information that he had carcinoma of the stomach and had been told that a radical operation might be possible, but that in any case an exploration should be done immediately. He had consulted Sir William Osler, hoping that he might have some other suggestion to make. The patient was quite emaciated, had a well-marked secondary anemia with a slight grade of jaundice, and showed a very definite tumor mass in the epigastrium. As a result of my examination I felt very doubtful of the diagnosis of carcinoma of the stomach, but I had no definite idea as to what the condition actually was. Sir William Osler's diagnosis was syphilis of the liver, the correctness of which was proved by the outcome. Under specific treatment the tumor disappeared with great rapidity and the patient gained rapidly in every way. He soon regained excellent health and has remained well from that time to the present.

The result in this patient illustrates one of the reasons why a more complete knowledge of syphilis of the liver is important. But for a correct diagnosis this patient would have had an abdominal section done, which would have been quite unnecessary. It is no uncommon thing to see patients with syphilis of the liver on whom an abdominal section has been performed, the diagnosis not always being made even after the abdomen has been opened.

The whole question of syphilis of the liver has been curiously neglected, and it is not strange that there is so little recognition

of the character of the tumor to which it gives rise. In the majority of cases there is either marked enlargement of the liver or a tumor mass of some kind is present. Thus in the 85 cases studied in this series only 5 were an exception to this. One general point is of particular interest and importance—this is the relatively greater involvement of the left lobe as compared with the right, a condition so marked that it should always excite suspicion of syphilis. This involvement of the left lobe was found in 48 cases of this series.

In a previous communication[1] I described the changes in the liver under three headings, and further experience has shown that these include the great majority of the cases. The forms are:

(1) General enlargement of the liver;
(2) Nodular masses;
(3) A rounded tumor.

It must be remembered that the stage at which the patient is examined must influence the occurrence of a tumor mass. The tendency is to cicatrization, and hence in late stages there may be marked deformity—with which the pathologist is usually more familiar than the clinician—or a cirrhotic process with notable contracture. But despite this tendency to the formation of scar tissue the liver may show enlargement or masses for a long period—in fact, it is difficult to set limits to the time. Some patients give definite histories of the tumor or the enlarged liver having been recognized many years before. This persistence of the enlargement for a long period is a striking feature.

Several other abdominal features are worthy of mention in association with a special discussion of the tumor. Among the symptoms *pain* is a common complaint, often severe, marked tenderness accompanying it frequently. Ascites had occurred or was present in 38 of the 85 cases, and both the duration and variability of this are striking. One patient had ascites at intervals over a period of eleven years, in which time tapping had been done seventeen times. The history of ascites which has been intermittent is particularly suggestive. *Splenic enlargement* is another frequent finding and was present in 54 of the cases. In the majority the increase in size is very marked, and this is a frequent cause of error, as the diagnosis of splenic anemia is made.

[1] *Am. Jour. Med. Sc.*, 1912, CXLIV, 625.

The various forms of change in the liver may be discussed in detail.

(1) *General Enlargement.* This was the most frequent form and was found in 39 cases. The extent of enlargement varies from a liver the edge of which is perhaps 2 inches below the costal margin to one which reaches below the level of the navel—an average increase being shown by finding the edge 3 or 4 inches below the costal margin in the right nipple line. The liver is usually hard, with a firm, rounded edge, and, as a rule, the left lobe shows relatively a greater increase in size than the right. Sometimes the left lobe presents a large rounded prominence in the epigastrium. In a few cases the surface may be slightly irregular, and occasionally there are well-marked fissures. In nearly all the cases of this group the liver is tender on palpation. In 15 cases there was distention of the surface veins and in 17 ascites was present.

It is easy to see how mistakes in diagnosis may arise. With an enlarged, tender liver, fever, and perhaps chills and sweats, a diagnosis of abscess of the liver may be made, while if there is cardiac disease with loss of compensation, the liver changes may be regarded as due to chronic passive congestion. But the most frequent error is to regard the condition as ordinary portal cirrhosis with enlargement. The mistake is the more easily made by reason of the occurrence of dilated surface veins and ascites. There are several features which are worthy of note. One is the persistence of the tumor. Such an enlargement may persist for years and be associated with ascites, which may increase and decrease. Some of the patients had been tapped at intervals over a period of years, which is quite contrary to the course of ordinary hepatic cirrhosis.

(2) *Nodular Masses.* These may occur practically in any part of the liver, but most often are found in the epigastrium or the adjoining right hypochondrium. In a certain number of cases they may be found over every part of the liver that is palpable. They usually occur in a liver which shows some general enlargement, but, as a rule, this is not as marked as in the first group. There were 21 cases of this form. Ascites occurred in 10 cases and prominence of the surface veins was marked in 8 cases. One point of some interest is the occurrence of a friction rub over these nodules. This was noted in a few instances and should always be kept in mind and looked for.

When one considers the many general symptoms that occur with syphilis of the liver, the possibilities of incorrect diagnosis in this form are very evident. With the loss in weight and marked anemia, the most likely mistake is to diagnose the condition as carcinoma. This diagnosis was made in several of the cases, in some of which it was only the lapse of time which proved it to be incorrect. In several others which I have seen an exploration had been done, the nodule being regarded as a tumor about the pylorus. Another possible error is to consider the enlargement as due to tuberculous peritonitis, the nodules in the epigastrium being regarded as representing an irregularly thickened omentum. The occurrence of ascites might easily increase the likelihood of this diagnosis.

There is one finding which should help to prevent error, and that is the enlargement of the spleen, which occurs so frequently with syphilis of the liver, and so rarely with such conditions as neoplasm and tuberculous peritonitis that it should be a safeguard against error. Unless a complete examination is made, however, the splenic enlargement may be missed entirely, especially if ascites is present. The enlargement of the left lobe of the liver being relatively greater than that of the right was generally manifested in this group, and is another aid against error.

(3) *Rounded Tumor.* This was found in 17 cases, and may be associated with general enlargement, but the most striking form is the large, smooth, rounded projection which is most likely to be found in the epigastrium. In some cases this was so marked that a large prominence was visible. In no instance were nodular masses found with this form, the surface being smooth; but occasionally a friction rub was heard over the mass. I have a very distinct recollection of the first case of this form which came under my observation. Nearly every man who examined it had a different suggestion; after the abdomen was opened the surgeon could not make a diagnosis; and the pathologist who examined a portion removed at operation could only say that there was some increase of the interstitial tissue. It is evident that with fever and possibly chills a diagnosis of abscess might easily be made; in general, however, the condition is usually regarded as a massive neoplasm. Only the passage of years may correct this, and then valuable time has been lost and the disease may

be beyond help. Ascites was present in 10 cases and an enlarged spleen in the same number.

(4) In a few instances the cases do not fall exactly into any of the preceding groups. If the condition has existed for some time and much fibroid change with shrinking has occurred, there may be no enlargement, and the irregular, hard left lobe may be felt in the epigastrium. It may not be possible to feel the edge of the liver in the right nipple line. Again, there may be a continuation of a nodular mass with marked irregularity of the left lobe. In general, it may be said that the changes usually come under one of the three forms described.

Errors in Diagnosis. These are discussed here only in so far as they result from the finding of nodular or rounded masses or the recognition of an enlarged liver. The errors are in one of two groups: (1) It is recognized that there is some diseased condition of the liver or gall bladder, but the nature of this is not diagnosed, or (2) the primary condition in the liver is not recognized, and is regarded as due to disease elsewhere. The result of error may always be serious in that a condition which usually yields to treatment is not recognized and time is given for further damage, while a further possibility is that an unjustified operation is done, both results fairly common in my experience. The delay in proper treatment may result in death, as shown by a case which was very striking, in which the patient died in three days after admission, and at autopsy it was found that the process had caused obliteration of the inferior vena cava and hepatic vein, with resulting thrombosis. The errors in diagnosis for which laparotomy is done are various. In some the condition was regarded as being cholelithiasis or cholecystitis, in others carcinoma, cyst, or abscess of the liver, or tuberculous peritonitis. Probably the most common error is to regard the case as one of ordinary cirrhosis with enlargement, the reason for which is very evident. A knowledge of the manifestations of syphilis of the liver is the greatest safeguard.

An error which had been made in several cases of this series was to regard them as *splenic anemia.* Naturally this occurred when the spleen was markedly enlarged, and the mistake was probably made because syphilis was not considered. It should be remembered that syphilis may cause a marked enlargement of the spleen. The point may be raised as to whether the liver is enlarged in splenic anemia.

My view is that this is unusual, and a marked increase in size should certainly arouse suspicion as to the correctness of such a diagnosis. The possibility of confusion from amyloid disease or an unusual form of Hodgkin's disease does not seem probable.

Congenital Syphilis. In all the cases of late congenital syphilis of the liver which have been recognized the tumor has been of the third form, that is, a large, rounded mass on a generally enlarged liver. As the age of occurrence is in childhood or youth, the condition is puzzling unless syphilis is considered. There were 5 such cases in the series.

SPLENIC ANEMIA

By W. J. Mayo, M.D., Rochester, Minn.

THE scientific vassalage of America to the Teutonic educational system has been the outstanding feature of American medicine for the last generation. The chief characteristic of this system, the delineation of minute details at the expense of perspective, has resulted in a loss of the sense of proportion in estimating the comparative values of the important and the unimportant manifestations of disease. The German method resulted in the accumulation of a mass of scientific facts, but it did not develop a well-devised system of accounting by which the more significant features of disease could properly be brought into prominence. Clinical medicine to-day is turning toward what might be called the British conception, by which a perspective of the disease is first obtained; that is, the disease is viewed as a whole, while emphasis is given to various characteristics according to their importance, and the patient rather than the collection of data is made the chief object of interest.

The name of Sir William Osler stands out pre-eminently among the men who have striven for a rational development of clinical medicine based on the central idea of curing the patient. Twenty years ago my attention was first called to splenic anemia by Osler's remarkable paper on this subject. His report of cases and his critical remarks, exhibiting a fine example of his clinical acumen, are still the best exposition in literature of the fundamental characteristics of splenic anemia, and definitely establish this name for a condition which for many years previously had been described under various titles.

Splenic anemia, as Osler pointed out, is a clinical entity. Its chief characteristics are an idiopathic enlargement of the spleen and a chronic progressive and intercurrent anemia which are the antecedents of phenomena related to portal circulatory obstruction, such as gastro-intestinal hemorrhage and ascites which eventually

cause death. If an attempt is made to study the clinical picture of splenic anemia in its minutiæ, it will be found that the picture fades quickly away, since its etiology is obscure and pathologically it presents no distinctive characteristics; only when it is seen as a whole and by exclusion is a diagnosis possible.

In 1866 Gretsel, in Griesinger's clinic, reported a case of splenic anemia in a child, and Griesinger, who termed the condition *anemia splenica*, had many such cases in adults. In 1871 H. C. Wood wrote on the subject; in 1885 Osler differentiated it in a discussion of the differential diagnosis of leukemia and pernicious anemia, and in 1899 Sippy made a critical summary of the literature. Since the publication of Osler's article in 1900 the principal advances in the investigation of the disease have been made in connection with the recognition of those conditions which, though they simulate splenic anemia, have been found to have a specific etiology. Hemolytic icterus, in which the jaundice was slight and intermittent, had been confused with splenic anemia. Occasional cases of pernicious anemia, in which the spleen was greatly enlarged, had also been thus improperly classified, not because the resemblance was striking, but because an enlarged spleen and the anemia were looked on as characteristic of the disease, and further investigation for the purpose of making a correct diagnosis was not continued. The splenomegalia of syphilis has also come to be recognized, and the enlarged spleen of chronic malaria, chronic sepsis, tuberculosis, and Gaucher's disease have been removed from the splenic anemia group as characteristic diagnostic features have developed. Various competent observers believe that von Jaksch's disease (infantile pseudoleukemia) is the infantile form of splenic anemia, in which the presence of a leukocytosis and abnormal marrow cells may be explained by the transitional characteristics of infants' blood (Giffin). Von Jaksch's disease is probably a syndrome produced by various infantile disorders. There still remains, however, an irreducible number of cases which present the clinical picture of splenic anemia and have an unknown etiology.

The chief pathological condition found in the spleen in splenic anemia is a generalized fibrosis. Deposits of connective tissue, compression atrophy of the malpighian corpuscles, and endophlebitis are the main features, and these are not grossly different from those

of the splenomegalia of syphilis, malaria, and other diseases of known origin associated with fibrotic spleens. The spleen of splenic anemia has been studied more carefully post-mortem, and this, I believe, has given rise to some misunderstanding of the condition of the organ when removed in the earlier stages of the disease.

Warthin and Dock have called attention to the importance of thrombosis of the splenic portal and mesenteric veins which have been found post-mortem. They believe that this condition is responsible for the ascites that occurs in some of these cases. Warthin showed, however, that ligation of the splenic vein produced atrophy and not enlargement of the spleen. In three cases in our experience in which death followed splenectomy for splenic anemia, marked ascites was present, while thrombosis of the superior mesenteric and portal vessels caused death. In one instance the thrombosis must have been of many months' or years' duration, as the patient had been ill for ten years and had had ascites for two years; the operation had been done in the last stages of exhaustion. Compensatory circulation in this case had been established through an extensive anastomosis about the occluded superior mesenteric vessels. The pathological change in the occluded vessels was of enormous extent, with the organization, apparently, of a clot that had become canalized, the final catastrophe completely blocking the circulation with fresh thrombi. There were no changes in the liver in this case, but in the other two cirrhotic changes were well marked.

Fibrotic Splenomegalia. An interesting feature of the conception of splenic anemia is the quite obvious attempt to split off from the disease all of those conditions in which the etiological factor is known, but which are otherwise characteristic. Unless gumma or the spirochete itself is found in the spleen, there is little about the fibrosis and vascular changes of syphilitic splenomegalia to distinguish it from the splenomegalia of splenic anemia; the anemia is quite the same. We have removed an enlarged spleen in chronic syphilis in five instances in which, by the most careful and prolonged treatment, we had been unable to cure the patient of syphilis or to reduce the splenomegalia to relieve the anemia; after the spleen was removed the patients were quickly cured. In three of these cases gumma was found in the liver at the time the spleen was

removed. Following the splenectomy antiluetic treatment proved to be much more effective, the liver became normal, and the patients have remained well for various periods up to five years (Giffin). The experience of Jonnesco in removing the spleen in the splenomegalias of chronic malaria and thereby promptly curing the patient of both the malaria and anemia again illustrates the therapeutic value of splenectomy.

The foregoing results lead to the belief that splenic anemia is a clinical entity, even when the cause is known, and that fibrotic splenomegalia produces anemia, irrespective of the initial cause of splenic enlargement. I am much in sympathy with this view. A patient with chronic splenomegalia who presents characteristics of chronic secondary anemia but who is not relieved by treatment is potentially a sufferer from splenic anemia, and will probably be cured by splenectomy without regard to the cause of the disease. This conclusion throws the burden of the production of chronic anemia on the spleen, while knowledge of the cause is unessential and may be even misleading, unless it leads to corrective treatment and renders eligible for surgical consideration any and all enlargements of the spleen in which anemia is the chief symptom. The anemia in the earlier stages may not be severe or continuous, the enlarged spleen may exist for months or years without anemia, but eventually the anemia becomes progressive and the secondary complications lead to death.

The Relation of Splenic Anemia to Banti's Disease. In 1883 Banti described a splenomegalia with chronic anemia associated with cirrhosis of the liver. In numerous communications since his original paper, Banti has added various diagnostic criteria which have still further obscured rather than clarified the subject. However, these criteria have made it possible to designate as Banti's disease almost any form of splenomegalia accompanied by anemia and liver changes in which a definite etiology cannot be established. Moschowitz, in a critical analysis of Banti's disease, came to the conclusion, with which I think nearly all observers will agree, that Banti's disease cannot be distinguished from splenic anemia, and that what is ordinarily called Banti's disease is a terminal stage which may be found in some cases of splenic anemia. That many patients die from splenic anemia without liver changes is certain.

That some patients have cirrhosis of the liver at an early stage of splenic anemia is equally certain. Some clinicians believe that all those conditions called splenic anemia in which cirrhosis of the liver is a prominent feature, are cases of primary cirrhosis of the liver, just as a still larger group of clinicians believe that cirrhosis of the liver is merely a terminal phase of splenic anemia. Personally, I have often been unable to determine in a given case of splenomegalia with cirrhosis of the liver and ascites whether the condition was primary in the liver or in the spleen. We are often forced to rely on the very indefinite history as to which was discovered first—the condition of the spleen or of the liver. Such data are, of course, wholly unreliable.

The spleen as normally situated in the average person must be nearly twice its normal size in order to be palpable, and the enlargement cannot, therefore, be definitely established until it reaches a weight of 300 or 400 grams, if we accept Sappey's estimate of 195 grams as the weight of the normal spleen. It should be borne in mind that considerable latitude must be permitted in estimating the size of the spleen; percussion to determine its size has, I believe, but little value. I have seldom found that the area defining the size and exact location of the spleen, marked out in advance by percussion, was corroborated by inspection after the abdomen was opened. And this is to a lesser degree true of our methods of ascertaining the size and condition of the liver, unless it can be palpated below the margin of the ribs. Therefore early diagnosis of the physical condition of the spleen and liver presents uncertainties which must be recognized.

Ascites, without changes in the liver, occurs in splenic anemia. The mere presence, therefore, of an ascites in connection with splenomegalia is not sufficient to demonstrate that the liver is at fault, although I believe it may be said that anemia is not a marked feature of primary cirrhosis of the liver even when ascites is present, while in splenic anemia it is an early and more or less continuous manifestation. It seems probable that certain as yet unidentified toxic agents strained out of the blood by the spleen are responsible for the fibrosis of the spleen and also for the cirrhosis of the liver.

Without going into the question of the physiology of the spleen, concerning which little is known, one may at least say that the frag-

mentation of worn-out red corpuscles is one of the spleen's functions and that when fibrotic it destroys an excessive number of red corpuscles, and this without regard to the etiology of the fibrosis, but probably does not interfere directly with blood production. The anemia is doubtless a "habit-anemia" (Rous) and simply an evidence of the gradual adaptation of the organism to a lower level of blood maintenance. The bone marrow is not markedly stimulated to overproduction, nor is there evidence of the toxic irritation of the bone marrow so characteristic of the so-called hemolytic anemias. Moreover, it may be that the pathologic changes of the disease actually reduce pigment production, which seems to be an important function of the liver, and in this way reduce the hemoglobin balance and foster the anemia.

It it also known that the spleen acts as a filter, removing bacteria from the blood stream, as in typhoid and tuberculosis; protozoa, as in syphilis and malaria, and undoubtedly other noxious agents. The spleen, unable to destroy these various substances, sends them through the splenic vein to the liver for destruction, and the reaction of the liver to chronic irritants is in the nature of a connective tissue disease which we speak of as cirrhosis without regard to its cause. If the spleen is unable to rid itself of all the material that it filters out of the blood stream sequestration of the filtrates may occur and give rise to the various splenomegalias with assured etiology, such as those due to the spirochete, plasmodium, typhoid bacillus, tuberculosis bacillus, and to others which have as yet no known etiology.

The spleen has differentiated and characteristic cells. It is therefore capable of varied pathological conditions. The liver has but one type of cells with different physiological activity, and its processes are less varied. The reaction of the liver to chronic irritation, reaching it by way of the portal system without regard to cause, is usually a fibrosis which we call portal cirrhosis.

The portal cirrhosis of Laënnec does not vary in type, whether produced by gin or pepper, or whether it is found locally about areas of tuberculosis, gumma, or cancer. Usually we have diagnosed cirrhosis with the hob-nail variety of Laënnec in mind. Yet in our experience, accepting fifty-five ounces as the weight of the average liver, the cirrhotic liver is as often enlarged as it is contracted.

As pointed out by Osler, the beer drinker and others may have huge, smooth, cirrhotic livers, in which the characteristic fibrosis is smoothed out by deposits of fat. On this assumption, therefore, we could say inferentially that the variety of splenic anemia which is accompanied by cirrhosis of the liver and has been called Banti's disease is a condition in which the fibrosis of the spleen and the fibrosis of the liver are due to the same agent, that they have a common etiology, and that the removal of the spleen when the disease is not too far advanced, cures the anemia by eliminating excessive blood destruction and relieves the liver of such substances as have been filtered from the blood stream so that the cirrhotic process in the liver itself is checked and the ascites disappears. We have patients, whose cases fulfilled this description, alive and in good health for years following splenectomy.

I have previously called attention to the fact that there is another element of relief following splenectomy which must be taken into consideration. In the normal condition 30 per cent of all the blood carried to the liver comes through the splenic vein, while in enormously enlarged spleens the splenic vein may be the size of the portal vein. The removal of the spleen in these cases relieves the liver of an overload, and it then becomes able to carry on its function without those evidences of circulatory obstructions that result in ascites and hemorrhages. Splenectomy may, therefore, be looked on as an equivalent to the establishment of an Eck's fistula or the condition we attempt to bring about by the establishment of collateral circulation, after the method of Talma, Morrison, and Drummond, through the vascular channels of Sappey, a condition described by Fagge as found with advanced cirrhosis in some person killed by accident while in apparent health.

Splenectomy. Splenectomy is the only curative treatment for splenic anemia. Radium and the *x*-ray have no such therapeutic successes as they have, for instance, in the palliation of leukemia. Iron, arsenic, etc., may be and undoubtedly are of importance in temporarily overcoming the more severe grades of anemia, and transfusion, following hemorrhages, is also of value. In the later stages, when serious circulatory changes such as endophlebitis, thrombosis, etc., have developed, the risk of operation is great and the prospect of cure is of course lessened. But even with these

terminal conditions, many patients have recovered their health and remained well for years following splenectomy.

Discomfort and pressure, from the size and weight of the spleen itself, and the anemia are the two conditions produced by the splenomegalia direct. It is self-evident that splenectomy relieves all those physical changes produced by the enlarged spleen, and removes the small but definite risk of splenic traumatism, (splenic) apoplexy, spontaneous rupture, and cystic degeneration. The enlarged spleen therefore has a certain pathological significance, and when not caused by an incurable condition, such as leukemia, or when not relieved by appropriate treatment in cases ordinarily considered curable, other things being equal, it should be removed. The clinical course of splenic anemia may be very slow and the anemia may not be continuous in the earlier stages; it has its ups and downs, and often for long periods of time the blood will be found approximating the normal. I have known persons, especially women, with enlarged spleens, to carry them for years without apparent symptoms, but eventually anemia has developed. In our experience after the removal of the spleen the anemia rapidly disappeared and the blood returned approximately to normal and so remained (Chabrol and Bénard).

Two conditions not so characteristic of fibrotic spleens in general but which are often associated with splenic anemia remain to be discussed, that is, hemorrhages, especially from the stomach, and ascites. A large majority of sudden and unexplained hemorrhages from the stomach in adult persons are the result of changes in the spleen or liver, or both, and the type of disease to be found in both the spleen and the liver is a fibrosis, more typical in the liver, because the liver has but a single kind of cell and therefore has less variation of pathology than the spleen, which has groups of specialized cells. Balfour has written most interestingly concerning the relation of the spleen to unexplained gastric hemorrhages, and has reported a remarkable case in which splenectomy restored to health a patient in the last stages of exhaustion from repeated hemorrhages extending over years. It is true that cases have been noted in which hemorrhages from the stomach have recurred after splenectomy, but in the majority of such cases hemorrhages do not recur.

For reasons that I have already pointed out the changes in the spleen, while of the same general nature as those in the liver, do not follow a specific and distinctive course similar to portal cirrhosis of the liver. The blood vessels in the spleen normally lose their middle and outer coats, and the blood, except for the endothelial coating of the blood vessels, comes in direct contact with the splenic pulp. We find, therefore, much greater changes in the blood vessels themselves than are found in the vessels of the portal circulation in hepatic cirrhosis. The patient with cirrhosis of the liver often has gastric hemorrhages and ascites, and usually comes to his death through portal circulatory obstructions. This is also true of the patient with splenic anemia, although the spleen in addition causes an anemia peculiar to itself. Forty per cent of the blood from the splenic artery goes to the stomach, being distributed largely about the fundus, and hemorrhages from the stomach may be due to some specific poison producing the gastric erosions of Dieulafoy, or more probably they are due to obstructed portal circulation producing definite back-pressure on gastric vessels distended through their strength. Removal of the spleen in this type of case may act by checking the distribution of toxic material or by reduction of the portal circulation, which forces the blood to travel around extra-hepatic channels directly into the general circulation. This applies equally to the ascites, which again is only another manifestation of the obstructed portal circulation.

The changes found at necropsy after death from splenic anemia are not necessarily to be considered the conditions that exist throughout the whole course of the disease; they are to a large extent terminal. Of 61 patients with splenic anemia from whom we removed the spleen 7 (11.7 per cent) died,[1] 3 from thrombosis of the superior mesenteric and portal veins, an acute condition superimposed on a previous canalized thrombosis having its seat in the splenic vein. These cases reproduced the picture seen at necropsy in the unoperated patient. All the patients operated on who were not in an advanced stage of the disease recovered and have remained well. We must therefore look on ascites, edema of the lower extremities, and cardio-renal decompensation as terminal conditions which

[1] These statistics extend to December 31, 1918, and include as operative deaths all patients dying in the hospital, without regard to cause of death or length of time after operation.

increase the dangers of operation. Yet the spleen may be removed successfully even in the terminal stage of the disease. We have operated on a number of patients for splenic anemia who had extensive cirrhosis of the liver, two of the Laënnec type. Following splenectomy the ascites disappeared and the hemorrhages from the stomach stopped; all who recovered from the operation are alive and apparently well after some years. The spleens in cases of splenic anemia are usually adherent and difficult to remove, and in the late cases when endophlebitis and thrombosis are marked the danger of an acute thrombosis of the large vessels of portal circulation is great. Eliminating the advanced cases the mortality from splenectomy for splenic anemia has been small.

REFERENCES

1. Balfour, D. C., "Splenectomy for Repeated Gastro-intestinal Hemorrhages." *Ann. Surg.*, 1917, LXV, 89–94.
2. Banti, G., "Dell anemia splenica," Firenze, 1882, 70 p. Repr. from; "Pubb. d. r. 1st di studi sup. . . . in Firenze. Sez. di med. e. chir."
3. Chabrol, E., and Bénard, H., "Present Status of Splenectomy," *Paris méd.*, 1918, VIII, 165. Abstr.: *J. Am. M. Ass.*, 1918, LXXI, 1865.
4. Dock, G., and Warthin, A. S., "A Clinical and Pathological Study of Two Cases of Splenic Anemia with Early and Late Stages of Cirrhosis." *Am. J. M. Sc.*, 1904, CXXVII, 24–55.
5. Fagge, C. H., "Principles and Practice of Medicine," Philadelphia, Blakiston, 1886, II, p. 304.
6. Giffin, H. Z., "Splenectomy for Splenic Anemia in Childhood and for the Splenic Anemia of Infancy," *Ann. Surg.*, 1915, LXII, 679–687; "The Treatment by Splenectomy of Splenomegaly with Anemia Associated with Syphilis," *Am. J. M. Sc.*, 1916, CLII, 5–16.
7. Gretsel, "Ein Fall von Anaemia splenica bei einem Kinde," *Berl. klin. Wchnschr.*, 1866, III, 212–214.
8. Jonnesco, T., "Splenectomie pour hypertrophie paludéenne," *Bull. et mém. Soc. de chir. de Bucarest*, 1899–1900, II, 3–7; 112; 1901–2, IV, 58; 64; also: *Internat. Clin.*, 1902, IV, 221–231.
9. Osler, W., "On Splenic Anemia," *Am. J. M. Sc.*, 1900, CXIX, 54–73: "Diseases of the Blood and Blood-glandular System," in Pepper, W., "System of Practical Medicine," Philadelphia, Lea, 1885, III, 882–950.

10. Moschowitz, E., "A Critique of Banti's Disease," *J. Am. M. Ass.*, 1917, LXIX, 1045–1051.
11. Sherren, J., "A Note on the Surgical Treatment of Certain Diseases by Splenectomy," *Ann. Surg.*, 1918, LXVIII, 379–382.
12. Sippy, B. W., "A Critical Summary of the Literature on Splenic Pseudoleukæmia (Anæmia Splenica; Splenomegalie Primitive)," *Am. J. M. Sc.*, 1899, CXVIII, 570–586.
13. Warthin, A. S., "The Relation of Thrombophlebitis of the Portal and Splenic Veins to Splenic Anemia and Banti's Disease," *Internat. Clin.*, 1910, 20 s., IV, 189–221.
14. Wood, H. C., Jr., "On the Relations of Leucocythemia and Pseudoleukemia," *Am. J. M. Sc.*, 1891, LXII, 679–687.

TUMOR FORMATION WITH PEPTIC ULCER

By Charles G. Stockton, Buffalo, N. Y.

CHRONIC peptic ulcer, especially near the pylorus, whether occurring in stomach or duodenum, often gives rise to tumor-like masses that arise from chronic inflammation, sometimes in connection with the process of slow perforation.

In rare instances these masses are carcinomatous; in others they are found to be largely inflammatory, but have elements of carcinoma in a limited area, or scattered through the growth; in the majority of cases they show no characteristics of neoplasm, and are purely inflammatory.

The gross appearance of these masses is much alike, whether carcinoma or inflammatory. In older cases, when carcinomatous, there may be expected metastases, direct invasion of neighboring organs, or both.

I have to describe a case which demonstrates that even without perforating, a chronic, duodenal, peptic ulcer may cause an inflammatory tumor that invades neighboring organs, replacing normal tissue in liver, pancreas, and intestinal wall, assuming the appearance in all respects characteristic of carcinoma; yet, upon microscopic study, the tumor is shown to be a fibrous mass of scar-like tissue, somewhat suggestive of keloid.

A physician, aged sixty years, had for two years suffered recurring attacks of epigastric pain, vomiting, and melena. In the intervals between attacks he had practiced his profession and taken solid food. On October 1, 1916, he entered the Buffalo General Hospital nearly exsanguinated, with marked gastrectasis from pyloric stenosis and spasm. One thousand c.c. of highly acid gastric juice was aspirated at one time. The case corresponded to those formerly classed as gastro-succorrhea from obstruction, and was characteristic of a benign process. There was a negative Wassermann reaction. There were no biliary symptoms. Under the effect of atropin a duodenal tube entered the intestine and duodenal feeding was employed with the hope of sufficient restoration to admit of surgical relief. Three

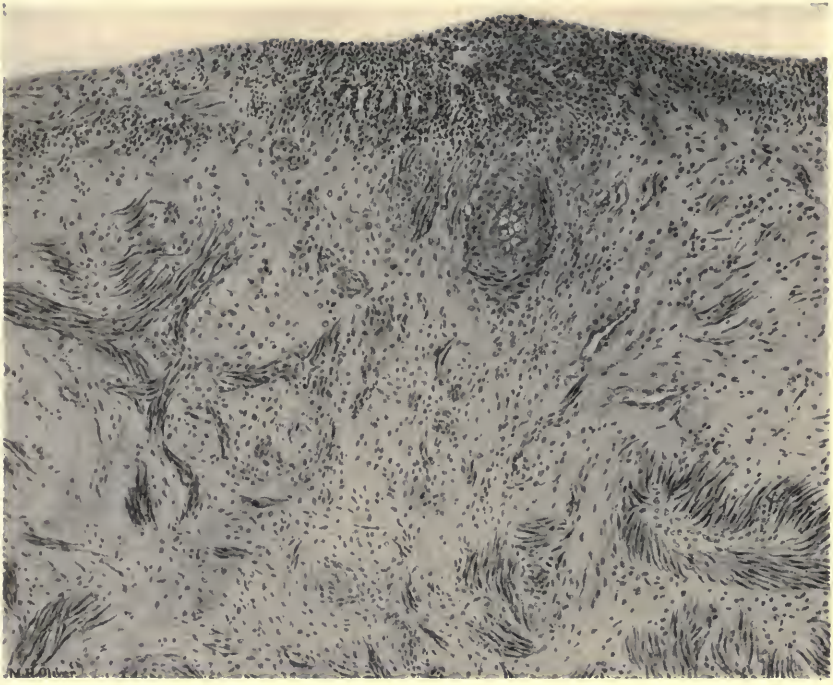

FIG. 1. INVASION OF THE WALL OF THE DUODENUM WITH NEW FORMED FIBROUS TISSUE; ATROPHY OF MUSCLE.

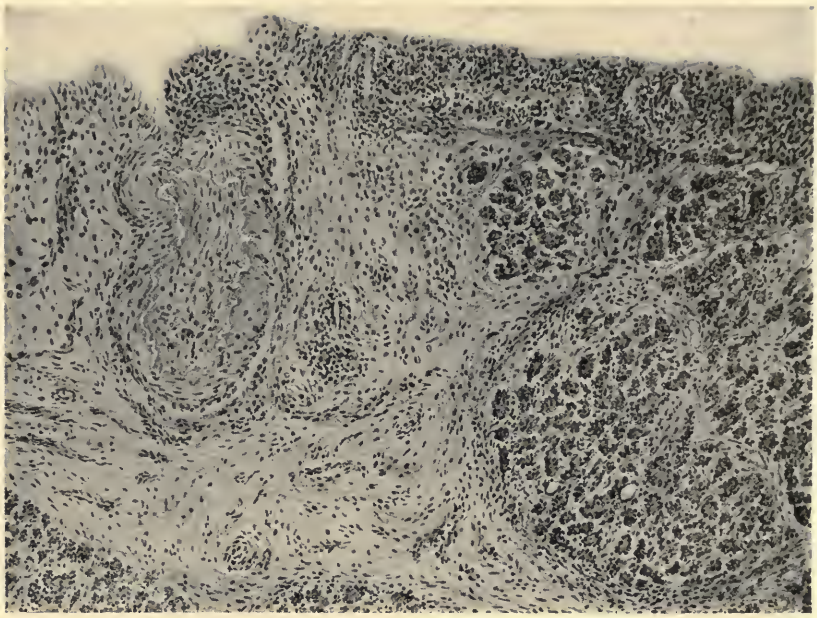

FIG. 2. NEW FORMED FIBROUS TISSUE EXTENDING BETWEEN THE LOBULES OF THE PANCREAS AND INVADING THE LOBULES.

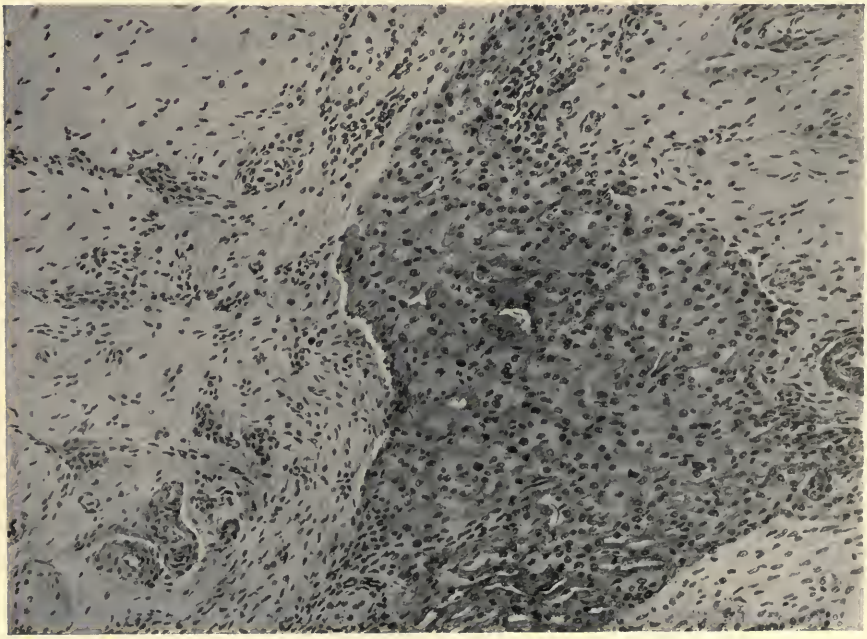

FIG. 3. NEW FORMED FIBROUS TISSUE SURROUNDING THE SMALL BILE DUCTS; INFLAMMATORY CELLS INVADING THE LOBULES.

hundred c.c. of blood was transfused. Marked improvement was seen for forty-eight hours, then the patient became delirious, dragged out the tube, went into collapse, and died of exhaustion, without further hemorrhage.

Autopsy. An irregular, nodular tumor was found invading the pylorus, the first portion of the duodenum, the head of the pancreas, the common bile duct (at its beginning and outlet), the duct of Wirsung, the gall bladder, and the contiguous portion of the liver. The cut surface was hard and cartilaginous. Posteriorly, near the pyloric ring, there was a deep, indurated, peptic ulcer largely occupied by a thrombus, about which was some bleeding. Although there were no metastases, the general appearance was that of carcinoma.

The microscopic examination by Dr. Herbert U. Williams revealed that there was exuberant connective tissue growth apparently replacing the normal tissue in pylorus, duodenum (Fig. 1), pancreas (Fig. 2), and liver (Fig. 3). The inflammatory cells not only invaded the muscle walls of stomach and duodenum, but the lobules of the pancreas and liver. The fibrous tissue extended along the bile radicles between the lobules of the liver, also the lobules of the pancreas. Small vessels were thrombosed. There were many much thickened capillaries showing hyalin degeneration. No evidence of cancer was discoverable.

The case was extraordinary in its general resemblance to cancer and in that the inflammatory tissue invaded the neighboring organs, replacing the normal tissue, thus resembling the method of neoplasm.

It is an interesting speculation as to what rôle the enzymes may play in the invading tendencies of inflammatory tumors of this kind.

ANEURYSM OF THE MIDDLE CEREBRAL ARTERY IN A CHILD NINE AND ONE-HALF YEARS OLD

By Fritz B. Talbot, M.D., Boston, Mass.

THIS child, nine years and eight months, was under observation for six years. His family history was negative. He was first seen December 24, 1908, for bronchitis at the age of four and one-half years, from which he rapidly recovered. In 1910 he had measles and was moderately sick. In the spring of 1911 he had whooping cough and whooped very badly. In November, 1912, he had an attack of asthma and was sick in bed for three or four days. In March, 1913, his appendix was removed. Since that time he had complained of tenderness about the head. Whenever the father ruffled his hair he said it caused considerable pain and made him feel sick, so that he had to go and lie down. These symptoms, however, were not severe enough to cause the parents to call in a physician. While at breakfast on February 26, 1914, he had slight nausea. He was taken out in the air and said he felt better and acted perfectly well the rest of the day. At 2 A.M. on February 27th he woke up, was nauseated and vomited and complained of pain in his head. The parents gave him ipecac and cleared out the bowels. Shortly after that he commenced to have convulsions. He was seen at 5 A.M. on February 27th and found to have a Babinsky and Kernig sign. The right pupil was very much contracted and pin-point in size. The left pupil was dilated, and the right side of the body was paralyzed. He had Cheyne-Stokes' respiration. His physical examination was otherwise normal. The convulsions became worse, and respiration stopped about 6 A.M. After he had artificial respiration for a few minutes he commenced breathing again. A lumbar puncture was done in the third inter-space and brought forth bloody fluid, which came drop by drop, without any pressure. About 20 c.c. was removed and the patient improved. It was believed that the blood was an accidental result of the lumbar puncture, and that the disease might be cerebro-spinal meningitis; 2 c.c. of anti-meningitis serum was, therefore, injected very slowly. This was discontinued, however, because the respirations again stopped, and artificial respiration was necessary. The needle was soon reintroduced into the spinal canal and more bright red blood obtained. This time there was no improvement in the symptoms. The patient died an hour later. The temperature twice taken by rectum was found to be normal.

POST-MORTEM EXAMINATION. The post-mortem examination was performed by Dr. Howard T. Karsner nine and a half hours later.

Body. Autopsy showed a body of a well-nourished, well-grown white boy with extreme rigor mortis. Incisions were limited to the head and back. Incision through scalp showed nothing unusual. The saw-cut through the skull released a great deal of fluid blood under pressure, and the entire vertex of the brain was found to be covered with blood, more particularly on the left side.

Brain. The pia appeared to show a very slight degree of roughening and was covered with blood. The vessels were much dilated and the sulci filled with blood. The base of the brain showed normal arteries, an enormous amount of blood under the pia and in the arachnoid, extending from a slight distance in front of the optic commissure to the medulla and laterally well up into the sylvian fissures. A single incision vertically through the brain showed a large amount of blood in the left ventricle.

The brain was suspended in formalin overnight and several more sections made on the morning of February 28th. These sections showed in the left hippocampus a cyst whose walls measured 1.5 mm. in thickness and about 2 cm. in diameter. The cyst was filled with fresh blood clot (proven fresh by histological section), and around the outer wall of the cyst was a large amount of fresh clot reaching to a depth of from 3 to 4 mm. As far as could be seen from the section, the hemorrhages appeared to have extended from this region up into the anterior cornu of the left ventricle.

Cord. The cord, upon removal, showed a considerable amount of fluid, under the pia and in the arachnoid, throughout its entire length. Transverse section showed a slight pink tinge about the gray matter. Histological section, on the morning of February 28th (frozen section), failed to show any sign of poliomyelitis.

Further examination of the fully hardened brain showed the cyst to be an aneurysm of the beginning of the middle cerebral artery. In the base of the brain this vessel could be seen, and upon dissection it was found to enlarge and form the aneurysmal sac. The anterior choroid artery could not be positively identified. Above and in the lateral aspect of the sac was found the continuation of the middle cerebral artery, and as it continued its course from the sac it almost immediately gave off the perforating branches and then the usual branches. The sac was irregular in its inner wall, but all the clot appeared to be fresh clot and there was no evidence of the brain substance having suffered from lack of nutrition. The clot around the sac was of varying depth, from 2 to 5 mm., and was fairly sharply defined from the brain tissue. The whole mass pushed upward

and outward the tissues of the anterior perforated space, and the temporosphenoidal lobe and the optic nerves and commissure appeared to be free from pressure. The coronal section of the optic thalamus showed a few large punctæ hemorrhagicæ, but no definite hemorrhage, and the remains of the brain substance failed to show hemorrhage.

The left lateral ventricle was filled and distended with blood, which also was found in the third and fourth ventricles. A perfect cast of the fourth ventricle was formed by the hardened clot. The clot showed that the blood extended into the foramen of Magendie. There was also a very small amount of blood in the right lateral ventricle.

No definite point of rupture of the sac could be made out, but it seemed most probable that the rupture was upward and into the anterior cornu of the lateral ventricle, and thence to the outer surface of the brain by way of the foramen of Magendie. A small area was found, however, in the inferior surface of the aneurysm which may have served as a point of origin of the external hemorrhage. This was sent through for histological examination.

Microscopical sections from various parts of the walls of the aneurysm were stained with hematoxylin and eosin phosphotungstic acid, hematoxylin and eosin, and by the elastica method. Additional sections from other parts of the brain were stained with hematoxylin and eosin.

The study of these sections showed the aneurysm wall to be made up largely of connective tissue, externally old and dense, internally younger, accompanied by new blood vessels and apparently of a sort of granulation tissue. At the point of origin of the aneurysm from the vessel, the elastica extended a short distance into the aneurysm wall, but was soon lost, and more remote parts of the aneurysms showed only a few fragments of curled elastic fibrils. Near the internal surface of the aneurysmal wall were found a few strands of fibrin enmeshed in the granulation tissue spoken of above. The muscular tissue of the artery extended into the aneurysm wall for about the same distance as the elastica, namely, about 3 mm., and was then lost.

A section of aneurysm wall was stained by the Levaditi method and examined thoroughly with oil immersion lens and mechanical stage and no treponemata found. Included in the sections were numerous large branches of the basal vessels of the brain, two of these showing well-marked thickening of the intima in focal areas. The perivascular lymphatics in places near the hemorrhage frequently contained blood, but there were no miliary aneurysms nor evidence of hemorrhage elsewhere into brain tissue. The section of supposed point of rupture of aneurysm showed nothing that could be safely interpreted as a point of rupture, although the

wall was very much thinned. Sections of spinal cord showed nothing abnormal.

The Wassermann reaction of the spinal fluid was slightly positive, but since the fluid was proven to be richly contaminated with *Bacillus coli communi*, the reaction must be considered of little value.

Summary. The case is regarded pathologically as an aneurysm following the vascular lesion of some acute infection. The sclerosis in this case is purely intimal in type and not the medial sclerosis of syphilis. As further arguments against syphilis are to be considered the practically negative Wassermann and the finding of no organisms by the Levaditi method; in addition must also be considered the absolutely negative history. On the basis of probability, vascular lesions in childhood are much more frequently the result of acute infections than of syphilis. If syphilis were present in the case it is hardly likely that it would have attacked only the arteries and left the patient well in other respects.

The rupture of the aneurysm may have been determined by the active exercise of the day with its concordant high blood pressure. The point of rupture could not be made out with certainty. Whether the rupture was through the inferior surface of the aneurysm or not, it seems certain that most of the blood passed into the left ventricle, and because of this fact it is presumed that the rupture was through the superomesial surface, into the left anterior horn, the left ventricle, the third and fourth ventricle, and thence into the pia arachnoid space.

Discussion. The diagnosis of aneurysm of the cerebral artery was, of course, not made during life, nor was it even suspected. When the lumbar puncture was performed the presence of bloody fluid gave a puzzling picture, as it was supposed that we were dealing either with a case of cerebrospinal meningitis, or infantile paralysis. The lumbar puncture very frequently results in blood-tinged fluid. The fact that the fluid continued to run bloody, however, and did not clear up at all, might be used as an argument against it being accidental, and that the blood had a causative connection with the illness. The cause, however, was not revealed until post-mortem examination.

The etiology of aneurysm of the cerebral artery shows that males are more frequently affected than females. Although the disease is most common in middle life, it is rarely ever found among infants and children. Osler reports a case in a lad of six, and other writers report aneurysm even in infants. Lebœuf (1) reported twenty-four cases of aneurysm in infancy which he had gathered from literature and were mostly aneurysm of the aorta. Phänomenow (2)

reported aneurysm of the abdominal aorta found while dissecting a fetus. Another case of aneurysm of the aorta was also reported by Durante (3) discovered in the same manner. It is believed by the French writers that there are two congenital aneurysms.

John Collins Warren (4) says that intra-cranial aneurysm is perhaps the most common variety of spontaneous aneurysm in children. He quotes Church, who published a table of thirteen cases in subjects under twenty years of age. In seven of these cases heart disease existed, and in six of these there were vegetations upon the valves. He regards this form of aneurysm as due to embolism and is inclined to think that disease of the arterial wall is rarely if ever a cause of the disease. West (5) reports a case of aneurysm of the left middle cerebral artery in a boy twelve years old following scarlet fever at eight years of age.

Speaking of aneurysm in general, Hochsinger (6) says that according to Liddell, who has grouped 243 special cases of aneurysm according to age, 7 occurred in children from two to five years of age; 1 from five to ten years, and 2 from ten to fifteen years; in all 10 during childhood. The disease, therefore, is rare in childhood.

The etiology in the case of this patient is not clear. Congenital syphilis can be practically excluded by the absence of a family history of miscarriages and infection of either parent, and by the lack of a strongly positive Wassermann. Thrombosis is ruled out by the post-mortem examination. The previous history of measles, whooping cough, and an infected appendix requiring operation, give the only clue to a possible source of infection of the arterial wall. None of these three diseases alone would seem enough to be the whole cause. It is possible, on the other hand, that the violent paroxysms of coughing during the pertussis may have weakened the arterial wall of the cerebral artery and made it more susceptible to infection. The suffusion of the face during severe paroxysms of coughing in pertussis and the frequently small hemorrhages inside the skull lend strength to this assumption.

The symptoms outlined are very obscure. It is possible that if the child had been examined during life with aneurysm in view, that it might have been diagnosed, but the slight symptoms of feeling bad because of his hair being ruffled did not lead the parents to consult a physician.

The treatment was, of course, absolutely hopeless, and one might wonder if the disease had been recognized ante-mortem whether any treatment could have resulted in repair.

BIBLIOGRAPHY

1. Lebœuf, Thèse de Bordeaux, 1898.
2. Phänomenow, *Arch. f. Gynaekol.*, 1881, XVII, 133.
3. Durante, Soc. anat., 1899.
4. Warren, John Collins, Keating, II, 868.
5. West, *Path. Trans.*, 1881, XXXII.
6. Hochsinger, Pfaundler and Schlossmann, "Diseases of Children," III, 521.

OBSERVATIONS ON CONGENITAL HYPERTROPHY OF THE PYLORUS

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THE clinical material on which the following remarks are founded consists in 100 consecutive cases of congenital pyloric hypertrophy which have been treated in hospital and private practice during the last twenty-five years (February, 1894, to February, 1919). A table of these is appended, and care has been taken to include in it only those cases in which the diagnosis seemed beyond a doubt. Of the 58 cases which ended fatally, 45 were examined post-mortem; and, of the remaining 13 in which this was not allowed, the condition of the pylorus had been ascertained during an operation in 4 instances.

The aim of the paper is to sum up briefly the writer's personal experience of a large number of cases, many of which were studied for an unusually long time. The subjects specially dealt with comprise the family history and complications, the causation of the muscular hypertrophy and of the symptoms, the natural course of the disease under medical and surgical treatment, the symptoms and choice of treatment in different types of the disease, the diagnosis, especially that between pyloric hypertrophy and the so-called "pyloric spasm," the difference in the prognosis in hospital and private cases, and the subsequent health of the patients who recover.

Family Occurrence. In one of the cases (No. 11) the father had suffered as a baby from similar symptoms. In another (No. 83) the mother's brother had died in infancy from what certainly seems to have been congenital pyloric hypertrophy. The father and paternal uncle of No. 13, who were Jews, had practised rumination since childhood.

In four instances there were two members of a family affected, namely Nos. 14 and 34; 24 and 29; 33 and 36; and 38 and 54. One of the patients (No. 86) was a twin, the other twin being normal.

Complications. In No. 36 there was a congenital heart-lesion. One patient (No. 46) whom I saw in consultation with Dr. D. B. Lees, was the subject of achondroplasia and died about a year later from hydrocephalus—long after the stomach symptoms had ceased. With these exceptions, no accompanying congenital malformations or diseases were observed.

One child (No. 96) was found on admission to hospital to be suffering from acute hæmorrhagic nephritis which was rapidly fatal. Another (No. 27) died from broncho-pneumonia ten days after admission to hospital.

The complication most to be feared is acute infective diarrhœa. When this occurs, as it is apt to do in a hospital ward during summer or autumn, the risk is very great; for children with pyloric hypertrophy seem to be peculiarly liable to suffer seriously from this form of infection. Three of the hospital cases (Nos. 54, 56, and 62) died from it while they were improving rapidly under medical treatment; one (No. 60), also treated medically, died two months after all his pyloric symptoms had ceased; and a third (No. 20) a month after a successful gastro-enterostomy.

In one case (No. 47) the patient, who ultimately did well, suffered for about three years after gastro-enterostomy from recurrent attacks of vomiting.

Causation of the Muscular Hypertrophy and of the Symptoms. The extended clinical and pathological experience which these cases have afforded has served to confirm former conclusions regarding its primarily nervous origin, although this does not seem to be the only cause of the obstruction.

When we examine the essential *structural* change that is present, we find that it is definitely restricted to the upper part of the alimentary tract and consists simply in a high degree of true hypertrophy of the entire muscular coat of the pylorus and adjacent stomach-wall, and a lesser amount of the same in the cardiac end of the stomach and in the œsophagus. The other local changes present, such as dilatation of the stomach and œsophagus, gastric catarrh, and general wasting of the body, are obviously secondary results of the pyloric obstruction.

The essential abnormality of *function* may be said to be similarly localised. It consists mainly in an ill-timed abnormally forcible and prolonged contraction of the pyloric muscle, which prevents the food passing into the bowel, and so accounts for the

starvation and wasting, the thirst and drying-up of the tissues, and the scantiness of the urine and fæces. In conjunction with the muscular hypertrophy of the stomach-wall it also explains the forcible vomiting.

While these facts can scarcely be disputed, there is still some difference of opinion regarding the origin of the muscular hypertrophy. Is the abnormal action of the pylorus and other parts a secondary phenomenon, due to the muscular coat being primarily affected by a simple congenital redundancy of growth, as Hirschsprung, Cautley, and others have suggested? Or, is the functional abnormality to be regarded as the primary element in the process—the muscle being hypertrophied merely because, from an early period of its development, it has been worried into overgrowth by constantly recurring overaction, such as would result from even a slight degree of habitual inco-ordination?

As these two hypotheses have been fully dealt with in a former paper (1) they need not be further discussed here. I may, however, give a brief statement of the second of them, which seems to me altogether the more likely of the two.

It is known that the normal fœtus swallows a considerable quantity of amniotic fluid during intra-uterine life; and, as this implies a certain amount of co-ordinated muscular action of the stomach and pylorus, it is believed that the supposed inco-ordination between these parts begins when the fluid first passes through them. There is reason to believe, however, that the muscular action may not at this period be very vigorous or continuous, and that therefore, by the time the child is born, only a small degree of hypertrophy will have occurred. After birth, when regular feeding has begun, the force of the muscular action and the inco-ordination will tend to increase so that the hypertrophy will progress much more rapidly than during intra-uterine life. It is in accordance with medical, surgical, and pathological experience that the pyloric tumour does grow larger and harder while the active symptoms continue. This is just what might be expected, for, as John Hunter pointed out long ago, a tendency to hypertrophy as the result of repeated forcible contractions is "a property of all muscles" and is greater in involuntary than in voluntary muscles. It is also extremely probable that tissue-growth of this sort is specially active in early infancy.

Fig. 1. Fig. 2.

Fig. 1. Transverse Section of Normal Pylorus near the Duodenum, × 4 Diam. Child of Nine Weeks.

Fig. 2. Transverse Section of Hypertrophied Pylorus near the Duodenum, × 4 Diam. Child of Nine Weeks.

Photographs by Mr. Richard Muir.

In the blocking of the pylorus there are two factors at work. There is first the abnormal muscular contraction, and, secondly, the mechanical effect of the increased bulk of the muscular tissue. This second factor is worthy of more attention than it has hitherto received.

When one contrasts a transverse section of a normal pylorus with one from a case of pyloric hypertrophy (Figs. 1 and 2), the degree to which the mere bulk of the hypertrophied muscle must diminish the pyloric lumen is obvious.

The muscular coat, as we have seen, grows quickly; but the peritoneal tube enlarges comparatively slowly with the general growth of the body, and is incapable of more than a moderate distension. The rapidly thickening muscle, therefore, presses more and more inwards as it grows, and the tube of mucous membrane is elongated and increasingly narrowed. The stage at which the symptoms become typical in any case probably depends mainly on when the muscular layer has become so thick that, even during relaxation, it seriously embarrasses the functional opening of the canal for the passage of food. As the rate of increase of the muscular hypertrophy varies in different children, there is a corresponding difference in the age at which severe obstructive symptoms occur. This is the apparent explanation why the violent vomiting sets in as early as the seventh or eighth day of life in some cases, while in others it does not occur until the sixth or eighth week.

The Natural Course of Recovery from the Disease. In considering the question of the treatment of pyloric hypertrophy, we have to bear in mind an important fact regarding its natural history which has been strongly emphasized by Robert Hutchison—that the disease is self-limited, in the sense that the pyloric lumen will eventually open up spontaneously and the child recover completely, provided he does not die in the process. When such spontaneous recovery occurs, we know from post-mortem experience that the muscular coat remains thickened for a long time, although its action has become gradually normal. Probably the muscular hypertrophy slowly lessens when the tendency to spasm has ceased, and doubtless the peritoneal tube goes on steadily widening also in the course of growth, so that the lumen of the pylorus becomes less

and less compressed; ultimately, the channel having become large enough for practical purposes, the passage of food takes place normally.

This natural opening-up of the lumen is usually a protracted, and often rather a risky process. Its progress is best estimated by watching the child's weight, which should if possible be taken daily throughout the illness. How it usually proceeds is seen in the accompanying series of weekly charts. These show the obstinate manner in which the weight often refuses to go up for many weeks after the medical treatment has begun, and the steadiness and rapidity with which it rises once the pyloric lumen has begun to widen. Evidently what we may expect from medical treatment in most cases, is not so much that we can greatly hasten the opening of the passage by what we do, as that we may be able to relieve it just sufficiently to keep the child alive, in spite of the continuance of the obstruction, until the natural process of recovery has had time to occur.

If the pyloric lumen is efficiently opened up by a surgical operation, however, the gain in weight usually sets in rapidly, as is seen in the weight-charts of Nos. 8, 81 and 90. Occasionally, as in No. 67, the channel has not been opened sufficiently by the operation, and symptoms of recovery do not begin till many weeks later.

The Symptoms and Treatment of the Different Types of the Disease. The choice of treatment in cases of congenital pyloric hypertrophy must depend to a large extent on the degree of severity of the case. This is ascertained partly from the history of the symptoms and the present condition of the child, but chiefly by investigating, in a preliminary way, the effect that regulation of the diet and stomach-washing have on the vomiting and on the gain in weight. According to the result of these measures we may class the cases as ordinary, acute, and mild.

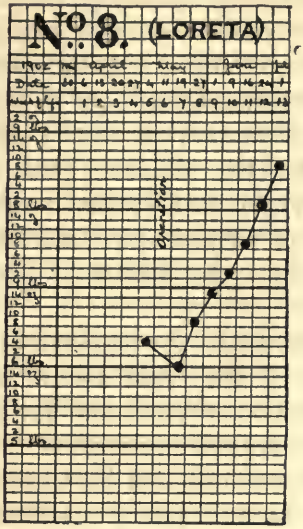
In the majority of cases of the *ordinary* type there is no vomiting at all during the first week or two of life, and the child gains in weight and vigour quite normally. In some, however, we are told that there has been, even from birth, an occasional "putting up" of a mild character—the milk being gently returned after the breast or bottle has been taken. Often the typical copious "shooting"

vomiting sets in quite suddenly without any apparent cause. The date of its onset varies, but it is very rare for it to begin during the first week, if indeed this ever occurs. It commonly starts between the second and fourth, and sometimes only appears as late as the sixth or eighth week. In five of my cases (Nos. 17, 39, 66, 83, and 87) the vomiting was never forcible. Once the violent vomiting begins, it usually continues at short intervals until special treatment is begun to stop it. The rapid loss of weight and the other signs of want of fluid absorption may set in, either before or after the characteristic vomiting.

When the usual symptoms are recognised, the preliminary treatment must begin at once. The size of the feeds should be restricted to 2 oz. or less, and the proportion of curd and fat in them lessened; and they should be given at regular intervals of two or three hours. At the same time, the stomach should be washed out with warm water once or twice a day. In this type of case such treatment almost always produces an immediate effect. The vomiting ceases, the child is much more comfortable, and he often begins to gain a little weight; although in most cases the symptoms recur whenever an attempt is made to increase the food given to anything like a normal amount.

Further treatment by hot fomentations over the stomach, and the administration of sedatives such as opium or belladonna, I have never found of much value.

A considerable proportion of hospital cases, and also some private ones are only brought for treatment after they have undergone a long course of unsuitable feeding, and the child is in a state of collapse, and has dilatation and catarrh of the stomach. Under these circumstances the most urgent indication is to stop all food for at least twenty-four hours, and to give subcutaneous injections of normal saline solution every four to six hours. The effect of these on the child's strength and comfort is very striking. Most infants bear them well, but there are a few whose subcutaneous tissues are so sensitive that the injections cause them considerable pain. Nutrient enemata are of no use, but it is always well if possible to supplement the subcutaneous injections by enemata of normal saline solution (one or two ounces every six hours). Some children are able for days to retain these without difficulty, but many resent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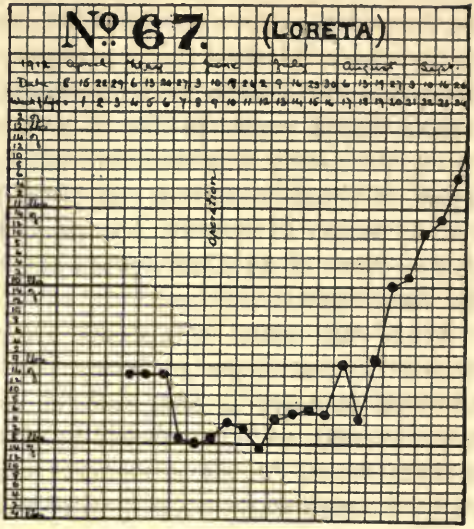
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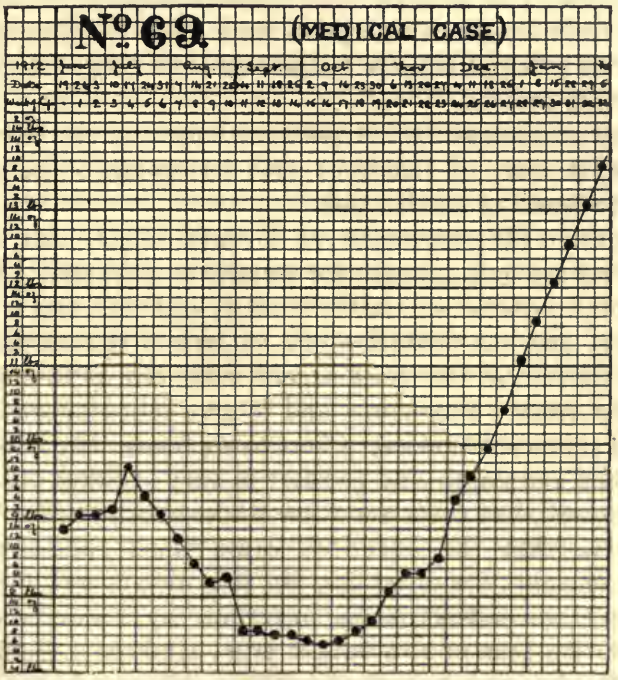

No. 69. (MEDICAL CASE)

them more than they do the subcutaneous infusions, so that they have to be given up.

If, after two or three weeks, the child is failing to respond to medical treatment, or sooner if he is rapidly losing strength, a surgical operation should be advised; and recent experience has shown that Rammstedt's operation is preferable in every respect to any other form of surgical procedure. It is very important that after the operation, and until recovery has set in, the case should continue to have the closest attention of both the physician and the surgeon.

In the *acute* cases the vomiting usually begins very early, and it sometimes becomes rapidly so urgent that not even a teaspoonful of water can be retained.

The first case of the disease I ever saw was a typical instance of this variety. (2) The patient (No. 1) throve fairly well on the bottle for the first ten days of life. Forcible vomiting set in suddenly on the eleventh day and persisted continuously, in spite of careful dieting and lavage, till the child died of inanition when he was twenty-eight days old.

This acute type is not often met with. Among the earlier reported cases, indeed, it figured to a fairly large extent, but that was because, at the time, the cases with milder symptoms were usually not recognised as instances of this disease. The fact that few except the worst cases were then diagnosed, accounts for the formerly expressed opinions that the disease is very rare indeed and that it never recovers without operation.

Whenever a case of pyloric hypertrophy proves by its failure to respond at all to preliminary treatment, to be of this type, it is advisable to have it operated on without delaying longer than is necessary to confirm the diagnosis; and it may occasionally be desirable, in typical cases, to call in the surgeon even before the characteristic visible peristalsis has begun, as was done in Nos. 34, 43, and 47. By doing so, we prevent the otherwise probable dilatation and catarrh of the stomach, and avoid further weakening of the patient before the operation. The degree of muscular hypertrophy is always, I think, considerable in these acute cases.

The very *mild* cases show an entirely different clinical picture. They are not at all uncommon, and it is probable that many of them recover with careful dieting only, and without a correct

diagnosis having ever been made. It is also probable that, if they were all recognised and suitably treated in the early stages, there would be many fewer dangerous examples of the ordinary type to be treated later. The increasing number of mild cases in recent reports must be remembered when we compare the older with the more recent statistics of the results of treatment. The mild cases are not generally seen by the physician until they are two or three months old, or later. They never require surgical treatment. The following (No. 37) is one of the most typical instances of this variety I have seen.

A girl of eleven weeks, who had thriven well on cow's milk during the first fortnight, but had since been kept rather thin by repeated attacks of what was thought to be dyspeptic vomiting, was found to have a large easily felt pylorus and extremely well-marked visible peristalsis. The recent feeding having been unsuitable in quality and excessive in amount, measured quantities of dilute peptonised milk were ordered. Stomach-washing was also recommended; but, for some reason, was not carried out. With this simple dieting and no other treatment, the child soon ceased to vomit, and began almost at once to gain weight at the rate of 4 ounces in the week; she is now a strong, healthy schoolgirl. In most of these cases, however, stomach-washing is necessary as well as dieting.

The symptoms in the mild cases differ only in degree from those in the severe ones and the physical signs are also the same, although they may be longer in appearing. The condition of the pylorus and stomach in the few instances in which I have seen them, either post-mortem or during an operation, were also practically the same. The mildness of the clinical manifestations, therefore, probably depends not on the pyloric muscle being less hypertrophied than in the worse cases, but on its being less frequently in a state of abnormal contraction, so that it allows a fair amount of food to pass into the bowel.

Diagnosis. Only in rare instances of the acute type can a satisfactory diagnosis of pyloric hypertrophy be made from the symptoms alone. Ordinarily we cannot recognise the nature of the case with certainty until we have observed exaggerated visible peristalsis, or made out the enlargement of the pylorus by palpation. In doubtful cases we should also use a stomach-tube to find

out whether a measured quantity of food—such as 2 ounces of diluted and peptonised milk—when introduced into the stomach and retained for three or four hours, remains undiminished in amount.

Exaggerated visible peristalsis occurring in a young baby, if it is really well-marked and forcible and accompanied by the characteristic vomiting and other symptoms, is always, so far as my experience goes, pathognomonic of the disease. It is most commonly seen for the first time during the fourth or fifth week, and is very rare indeed before the end of the third. Often, it begins much later, and it may go on vigorously after the vomiting has ceased. At first, it may only appear irregularly at intervals of hours or even of days.

The large hard pylorus can often be felt some time before the visible peristalsis has begun, but in none of my cases was it made out for certain before the eighteenth day of life. The organ sometimes lies too deeply under the liver to be felt even during anæsthesia; and, although it is in an accessible position, it may not be possible to make sure of its presence unless it is in a state of contraction at the time of examination. I have never found it necessary to use *x*-ray examination as an aid in the diagnosis of this disease.

The cases which are most apt to be mistaken for pyloric hypertrophy are those of an obscure nervous condition which has been usually referred to as "pyloric spasm." Mild instances of this malady are not uncommon and generally give little trouble, because the vomiting and other symptoms are much less severe than those in pyloric hypertrophy, and generally subside rapidly when the feeding is regulated and the stomach washed out. In a few of the cases, however, the symptoms are extraordinarily obstinate and, in these, the diagnosis, and especially the treatment, may be very troublesome.

The worst cases I have seen have generally been in girls, and it is characteristic of the condition that the child often cries a great deal as if in pain, which children with pyloric hypertrophy rarely do. The vomiting usually begins soon after birth, but does not become projectile until some time between the end of the second and the sixth week. Its character differs somewhat from that in pyloric hypertrophy. It generally occurs after each feeding, and the

whole stomach contents are either forcibly rejected at once, or the organ is emptied by successive less severe efforts. When the stomach-tube is used after vomiting has taken place, little or no residue of food is found in the stomach, and there is no evidence of gastric dilatation or hypertrophy. Occasionally, before vomiting occurs, the outline of the stomach stands out distinctly, but it never shows the characteristic vigorous peristalsis. The motions and the urine are usually scanty, but slight attacks of diarrhœa are quite common.

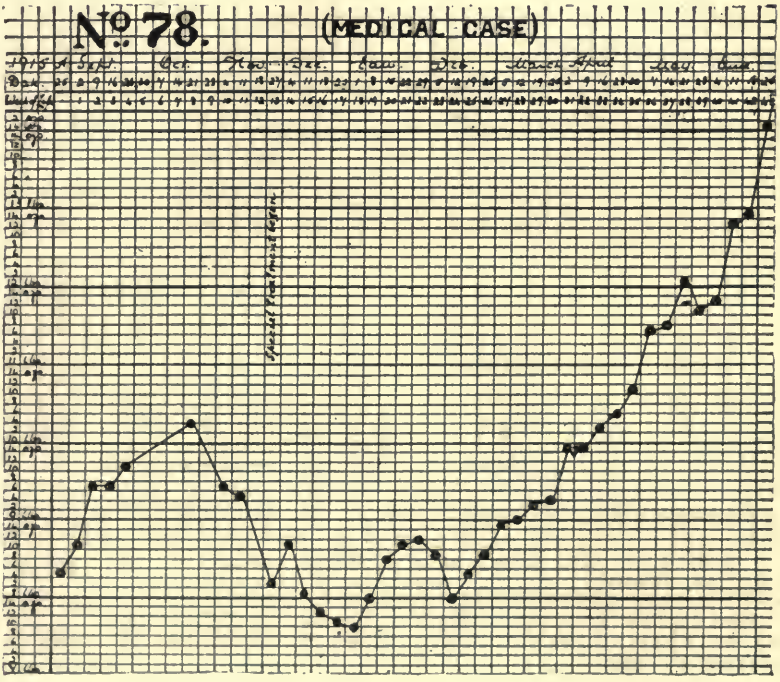
The treatment of these cases requires the greatest care and perseverance. Suitable regulation of the diet is, of course, necessary, and stomach-washing should be regularly carried out; but often neither the one nor the other has any strikingly beneficial effect on the habitual return of the meals. The most useful treatment, in my experience, has been the cautious use of tincture of opium, beginning with doses of m. $\frac{1}{40}$ and rapidly increasing to m. $\frac{1}{10}$ or even m. $\frac{1}{5}$. Under this the vomiting gradually stops and the weight increases. If the mother is careful, the case often does better at home than in hospital, and home treatment is also preferable because these cases, like those of pyloric hypertrophy, are apt to die if they contract infective diarrhœa. On post-mortem examination, the pylorus and stomach are found to be quite normal.

Cases of congenital narrowing of the second part of the duodenum with saccular dilatation of its first portion are sometimes mistaken for pyloric hypertrophy. In this condition, visible gastric peristalsis is sometimes seen, but it is not very forcible. It may also appear in the first week of life, which that in pyloric hypertrophy never does. The vomiting, also, is not forcibly projectile and the child is feeble, and does not thrive well during the first few weeks, as cases of pyloric hypertrophy almost invariably do.

Mortality with Different Forms of Treatment in Hospital and in Private Practice. Out of the 100 cases, 42 recovered, and 58 died either of the disease or of complications.

Operations were performed in 39 cases, of these 16 (i.e., 41 per cent) recovered, and 23 (i.e., 59 per cent) died. The operations were of various kinds. Pylorectomy and pyloroplasty were done each in 1 case; and both patients died; gastro-enterostomy in 12 children, of whom 3 recovered (i. e., 25 per cent); divulsion of the py-

lorus (Loreta's operation) in 18, with 7 recoveries (i. e., 38.9 per cent); in 2 others, Loreta's operation failed to relieve the symptoms and was therefore followed by gastro-enterostomy, after which both patients made a good recovery; simple division of the pylorus muscle, without stitching (Rammstedt's operation) was done in 5 cases, with 4 recoveries (i.e., 80 per cent). The cases which recovered were all operated on by Sir Harold Stiles, with the exception of



Nos. 95 and 97, in which the operations were performed by Mr. A. P. Mitchell and Mr. John Fraser respectively.

Of the 61 cases in which no operation was done, 1 (No. 96) died a few days after admission to hospital from acute nephritis of unknown origin, and 6 others (Nos. 6, 13, 17, 32, 94 and 100), who were in a state of extreme collapse when first seen, died rapidly from exhaustion, most of them within forty-eight hours and one on the fifth day. Of the remaining 54 cases that were medically treated, 26 (i.e., 48 per cent) recovered; and 28 (i.e., 52 per cent) died. In 3 of the latter, death was caused by infective diarrhœa.

Number of Case.	Date First Seen.	Sex.	Hospital or Private Patient.	Age in Days when First Seen.	Age in Days at Onset of Forcible Vomiting.	Order of Child in Family.	If Operated on.	Nature of Operation.	Recovery or Death.	If Examined P. M.	Remarks.	Age in Years in Feb., 1919.
1	Feb., 1894	M	P	18	11	9	O	——	D	X	Very acute case.	—
2	Mar., 1896	M	P	66	28	4	O	——	D	X		—
3	April, 1896	F	P	27	?8	2	O	——	D	X		—
4	Feb., 1900	F	H	52	?	6	X	Pylorectomy	D	X		—
5	Mar., 1900	M	P	35	14	1	X	Gastro-Enterostomy	D	X		—
6	Mar., 1900	F	H	49	28	2	O	——	D	X	Collapse on admission. Convulsions. Death within two days.	—
7	Mar., 1902	F	H	24	12	3	X	Loreta	D	X		—
8	April, 1902	M	H	32	17	1	X	Loreta	Rec.	—	Now healthy and vigorous. In regular work.	16¾
9	July, 1902	M	P	54	33	1	X	Loreta	Rec.	—	Now a strong, healthy public-school boy. No indigestion.	16½
10	Nov., 1902	M	H	38	9	3	X	Loreta	D	X		—
11	Nov., 1902	M	P	32	?28	1	O	——	Rec.	—	Now strong and healthy.	16¼
12	April, 1903	M	H	25	?	9	X	Loreta	D	X		—
13	April, 1903	M	H	123	14	4	O	——	D	X	Collapse on admission. Died within a few hours.	—
14	May, 1903	M	P	34	?32	1	X	Loreta	D	X	Constant high temperature (over 104° F.) and diarrhœa before operation.	—
15	June, 1903	M	P	69	47	3	X	Loreta and Gastro-Enterostomy	Rec.	—	Died two years after from septic infection of throat.	—
16	April, 1904	M	P	49	?	1	X	Gastro-Enterostomy	Rec.	—	Now a healthy schoolboy.	14¾
17	Aug., 1904	M	P	81	never forcible	4	O	——	D	X	Collapsed and died after a series of convulsions.	—

18	Aug., 1904	F	H	42	7	1	X	Gastro-Enterostomy	D	X		—
19	Sept., 1904	M	H	53	21	3	X	Gastro-Enterostomy	Rec.	—	Now a big, strong boy. Splendid appetite, never ill.	14½
20	Oct., 1904	M	H	49	21	4	X	Gastro-Enterostomy	Rec.	X	Died one month later from infective diarrhœa.	—
21	Oct., 1904	M	H	49	?	4	X	Gastro-Enterostomy	D	X	Collapsed and died at end of operation.	—
22	Feb., 1905	F	H	36	14	4	X	Gastro-Enterostomy	D	X		—
23	Mar., 1905	M	H	28	16	2	X	Loreta	D	O		—
24	Mar., 1905	M	H	99	?25	2	O	——	D	O		—
25	May, 1905	M	H	28	10	1	X	Pyloroplasty	D	X		—
26	May, 1905	M	H	42	?	4	X	Gastro-Enterostomy	D	X		—
27	Sept., 1905	M	H	43	14	2	O	——	D	X	Died of broncho-pneumonia after ten days in hospital.	—
28	Nov., 1905	M	H	54	?28	5	O	——	D	X		—
29	Jan., 1906	M	H	22	?28	3	X	Gastro-Enterostomy	D	X		—
30	Feb., 1906	M	H	92	?	1	O	——	Rec.	—	Parents were tramps. Child lost sight of within six months.	(13¼)
31	April, 1906	M	H	49	14	4	X	Gastro-Enterostomy	D	X		—
32	May, 1906	M	H	31	?	7	O	——	D	X	Was collapsed on admission and never recovered.	—
33	May, 1906	M	H	34	25	5	O	——	D	X		—
34	July, 1906	F	P	14	12	3	X	Loreta	Rec.	—	Now well-grown, full of life. Used to have "liver-attacks." Not now.	12½
35	Mar., 1907	M	H	84	25	3	O	——	Rec.	—	Now a fine, big, healthy boy. No indigestion, occasional headaches.	12
36	May, 1907	F	H	21	11	6	O	——	Rec.	—	Congenital heart-disease. Very cyanotic. Well nourished.	11½
37	June, 1907	F	P	75	?56	?	O	——	Rec.	—	Now a healthy schoolgirl. Very athletic. No indigestion.	11¾

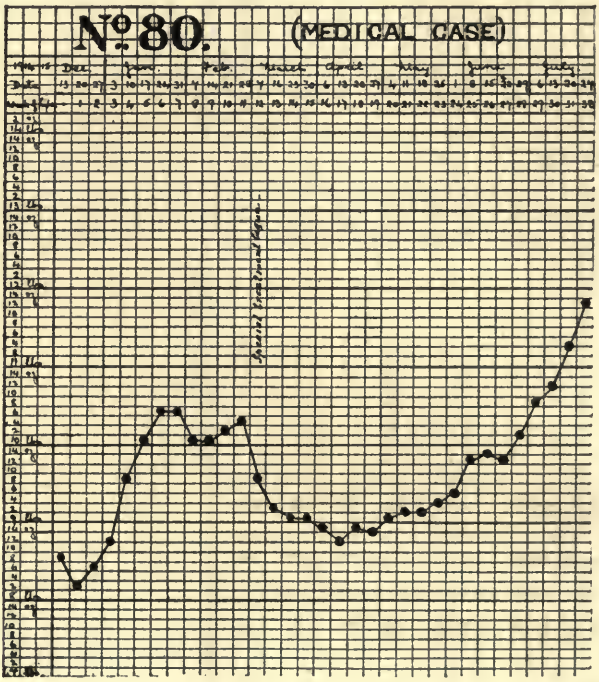
Number of Case.	Date First Seen.	Sex.	Hospital or Private Patient.	Age in Days When First Seen.	Age in Days at Onset of Forcible Vomiting.	Order of Child in Family.	If Operated On.	Nature of Operation.	Recovery or Death.	If Examined P. M.	Remarks.	Age in Years in Feb., 1919.
38	July, 1907	M	H	48	none	4	X	Loreta	D	X		—
39	July, 1907	M	H	49	32	1	X	Loreta	D	X		—
40	July, 1907	M	H	25	18	1	X	Loreta	D	X		—
41	July, 1907	M	H	70	40	1	O	——	Rec.	—	Did well for seven months, then parents went to Australia.	(11½)
42	Dec., 1907	M	H	66	14	5	O	——	D	O		—
43	Jan., 1908	M	P	19	14	1	X	Loreta	Rec.	—	Now strong, though thin. No indigestion. Enlarged cervical gland.	11
44	Feb., 1908	M	P	65	14	2	O	——	Rec.	—	Now a very well-nourished healthy schoolboy.	11
45	April, 1908	M	P	90	21	3	O	——	Rec.	—	Now a big, strong, healthy-looking boy.	11 11
46	May, 1908	M	P	112	21	2	O	——	Rec.	—	Achondroplasic. Died of hydrocephalus a year later.	—
47	Aug., 1908	M	P	21	12	1	X	Loreta and Gastro-Enterostomy	Rec.	—	Recurrent vomiting for about three years. Now strong and healthy.	10½
48	Oct., 1908	M	H	56	40	2	O	—— ——	Rec.	—	Was quite well four years ago when parents went abroad	(8½) —
49	Aug., 1909	M	H	31	?	1	O	——	D	X		—
50	Sept., 1909	F	H	77	42	1	O	——	D	O	Diarrhœa.	—
51	Jan., 1910	M	H	56	35	5	O	——	D	X		—
52	Feb., 1910	M	H	63	42	1	O	——	D	X		—

53	April, 1910	M	P	54	12	1	O	——	Rec.	—	Now a healthy boy with no dyspepsia.	9
54	July, 1910	M	H	56	53	5	O	——	D	O	Died from infective diarrhœa.	—
55	Oct., 1910	F	P	26	21	1	O	——	Rec.	—	Now a big, fat, healthy child. Occasional flatulence.	8½
56	Oct., 1910	M	H	59	31	4	O	——	D	X	Died from infective diarrhœa.	—
57	Oct., 1910	F	H	30	?8	1	O	——	D	X		—
58	April, 1911	M	H	24	11	2	O	——	D	X		—
59	May, 1911	F	H	120	21	10	O	——	D	X		—
60	May, 1911	M	H	30	18	1	O	——	Rec.	X	Died from infective diarrhœa two months after vomiting had ceased.	—
61	May, 1911	M	H	89	32	3	X	Gastro-Enterostomy	D	O		—
62	July, 1911	M	H	59	?8	1	O	——	D	X	Died from infective diarrhœa two months after admission.	—
63	Nov., 1911	M	H	21	10	2	X	Loreta	Rec.	—	Now a very healthy boy in every respect.	7½
64	April, 1912	M	P	92	30	3	O	——	Rec.	—	Now in excellent health, occasional flatulence.	7
65	May, 1912	F	H	54	10	2	O	——	D	O		—
66	May, 1912	M	P	31	10	1	O	——	Rec.	—	Now in good health. Occasional slight indigestion and hiccough.	6¾
67	June, 1912	M	H	61	14	2	X	Loreta	Rec.	—	Now very healthy. A hearty eater.	6¾
68	July, 1912	M	P	265	10	2	O	——	Rec.	—	Very strong and healthy at five years. Since lost sight of.	(7¼)
69	July, 1912	M	P	42	35	2	O	——	Rec.	—	Now well-nourished. Slight eczema and recurrent bronchitis.	6½
70	April, 1913	F	H	84	?7	1	O	——	Rec.	—	Now health is excellent. No indigestion.	6
71	Sept., 1913	M	H	28	7	2	O	——	D	X		—

Number of Case.	Date First Seen.	Sex.	Hospital or Private Patient.	Age in Days When First Seen.	Age in Days at Onset of Forcible Vomiting.	Order of Child in Family.	If Operated On.	Nature of Operation.	Recovery or Death.	If Examined P.M.	Remarks.	Age in Years in Feb., 1919.
72	Dec., 1913	M	P	82	20	5	O	——	Rec.	—	Now is very strong and well.	5¼
73	Feb., 1914	M	H	34	15	1	O	——	D	X		—
74	Mar., 1914	M	H	35	?	1	O	——	D	O		—
75	April, 1914	M	H	42	?	?	X	Loreta	D	X		—
76	June, 1914	M	H	49	?	?	X	Gastro-Enterostomy	D	X		—
77	June, 1914	M	H	41	?	?	O	——	D	X		—
78	Nov., 1914	M	P	85	41	1	O	——	Rec.	—	Did very well; but died twelve months later from tuberculous meningitis.	—
79	Mar., 1915	M	H	59	38	6	O	——	Rec.	—	Wretched home. Large family. Rickety and poorly nourished like the other children.	4
80	Mar., 1915	M	P	85	21	1	O	——	Rec.	—	No illness since infancy. Very strong and well.	4
81	Mar., 1915	M	P	32	22	1	X	Loreta	Rec.	—	Now a strong, healthy boy.	4
82	Mar., 1915	M	P	62	28	1	O	——	Rec.	—	Now splendidly healthy. Occasional slight "bilious attacks."	4
83	April, 1915	M	P	26	never	1	O	——	Rec.	—	Now a strong, fat, healthy child.	3¾
84	June, 1915	M	P	33	27	2	O	——	D	O		—
85	June, 1915	M	P	41	14	1	O	——	D	O		—
86	Nov., 1915	M	H	27	22	1	X	Loreta	D	O		—
						twin						
87	Nov., 1915	M	H	24	never	1	X	Loreta	D	X		—

88	Mar., 1916	M	P	49	37	3	X	Rammstedt	Rec.	—	Now a big, fat child, and well in every way.	3
89	May, 1916	M	H	43	14	7	X	Rammstedt	D	O		—
90	July, 1916	F	P	84	15	3	X	Rammstedt	Rec.	—	"Splendidly well," but will not take solid food.	2¾
91	Sept., 1916	M	H	24	7	1	O	——	D	O		—
92	Oct., 1916	M	H	49	21	9	O	——	D	X		—
93	Oct., 1916	M	H	84	42	2	O	——	D	X		—
94	Feb., 1917	F	H	135	21	1	O	——	D	O	Admitted in state of collapse and died in a few hours.	—
95	Mar., 1917	M	H	46	28	2	X	Rammstedt.	Rec.	—	Now is a "splendid boy."	2
96	Sept., 1917	M	H	59	35	7	O	——	D	X	Found on admission to have acute hæmorrhagic nephritis.	—
97	Oct., 1917	M	H	70	42	2	X	Rammstedt	Rec.	—	Now "the finest specimen of his age in the district."	1½
98	Nov., 1917	M	P	70	?	5	O	——	Rec.	—	Now a robust baby. The digestion perfectly good.	1½
99	May, 1918	M	P	28	10	3	O	——	Rec.	—	Now strong and well in every way.	¾
100	June, 1918	M	P	84	14	2	O	——	D	O	In a state of collapse when first seen.	—

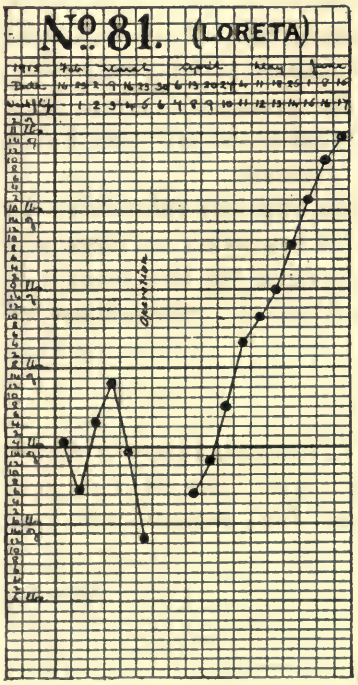
The most remarkable thing about the mortality statistics is the striking difference between the results obtained in hospital and those in private practice. For we find that the total mortality of the 28 hospital cases which were operated on was 75 per cent (21 deaths), and that of the 11 private cases 18.2 per cent (2 deaths). In the same way, if we exclude the 7 cases which died within a few days of being first seen and before the treatment could be

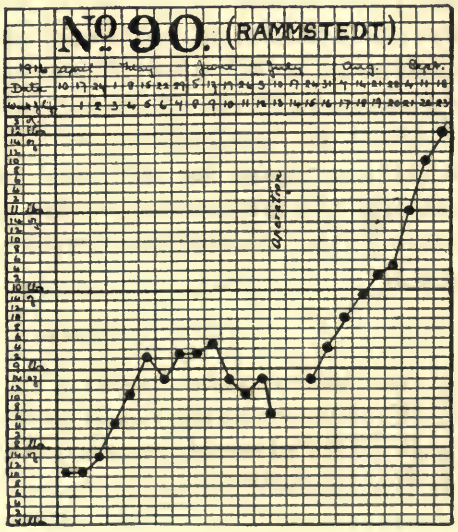


properly begun, we find that while the 31 hospital cases which were medically treated show a mortality of 74.2 per cent (23 deaths), that of the 23 cases similarly dealt with in private practice was only 21.7 per cent (5 deaths).

There are at least three obvious reasons for this great difference. The first of these is the state of debility in which many of the hospital cases were on admission, owing to previous injudicious feeding. This had set up gastric catarrh and dilatation, sometimes with diarrhœa, and had lowered the child's resistance. In former years, the nature of the case had rarely been recognised before the patient

was brought to the hospital. The second is the danger of infective diarrhœa, which sometimes occurs in hospital and practically never in private practice. The third reason is that it is seldom possible to give anything like the same amount of medical and nursing attention to the hospital cases as in private practice. In the latter, one has usually been able, when the case was a severe one, to arrange for the child to be looked after both by day and at night by specially





competent nurses, who have given their whole time and attention to him. I have also made a point of doing the washing out of the stomach myself or having it done by another medical man. This I believe to be important, for it not only results in the washing-out being better done, but also often in information being obtained which may be most helpful in the regulation of the diet. If the lavage is carried out by nurses, I am convinced that this may considerably lessen the chance of the child's recovery.

Condition in After-life of the Patients who Recover. Of the 42 children who recovered, 5 (Nos. 15, 20, 46, 60 and 78) have since

died from various causes, and 4 (Nos. 30, 41, 48 and 68) who were doing well when last seen, have been lost sight of. During January and February of this year I have been able to see a number of the remaining 33 patients and have had reports on all the others, either from their medical attendants or from relatives. The present ages of these children vary from ten months to 16¾ years. The majority, doubtless owing to the extra care which their mothers have taken of them, are above the average in development and vigour; none shows any signs of serious gastric derangement. Apparently the danger to life and even to health in this disease is only temporary, and children who survive it in infancy are in no way handicapped thereby in after-life. Those who were operated on are now apparently as well as the others who were medically treated.

Mr. J. H. Nicoll allows me to mention that Dr. John Ritchie's patient, on whom he performed Loreta's operation in 1899, and who was the first successful case of operation for this disease in Great Britain (3), was examined for the Army last year and passed as A 1.

BIBLIOGRAPHY

1. "On Defective Co-ordination in Utero as a Probable Factor in the Causation of Certain Congenital Malformations." *Brit. M. J.*, II, 678.
2. *Brit. M. J.*, 1895, II, 711, and *Edinb. Hosp. Rep.*, 1896, IV. 116.
3. *Brit. M. J.*, 1900, II, 571.

THE CARDIOVASCULAR DEFECTIVE

By Louis M. Warfield, A.B., M.D., Milwaukee, Wis.

THE examination of thousands of young men for military service during the late war has drawn attention to a group of symptoms following exertion of the slightest kind, known by such synonyms as effort syndrome, irritable heart, neuro-circulatory asthenia, etc. The English tagged their cases from the "front" D.A.H. (disordered action of the heart), but as time went on it became evident that attention thus drawn to the heart made the victims worse, so that Thomas Lewis proposed the name "effort syndrome." The cases which were invalided from the front and those seen in civil life have the same syndrome. The difference, if any, is one of degree. It is to the class of cases seen in civil life that the name "cardiovascular defective" is given in this paper.

Certain characteristic symptoms are found in all cases of the cardiovascular defective. These are symptoms from which many men suffer when put through violent exertion. The differentiation between the defectives and the normal men is largely one of degree. Exercise of the lightest character serves to bring out in the defectives an exaggeration of all the symptoms of exhaustion. Typically, after slight exertion the men become breathless, giddy, have pain over the precordium, palpitation of the heart, and have a feeling of utter exhaustion. Frequently they have headache, are sleepless, rest at night really does not rest them, and they have clammy cyanosed hands and feet. They sweat profusely in the axillæ and have a mottled skin and unstable vasomotor reaction.

This train of symptoms follows practically every serious illness and lasts for a long or short time, depending upon the recuperative powers of the person affected and upon the severity of the illness. This is to be expected and causes no anxiety. It is only when the time has passed that recovery should be perfect and symptoms still

persist that permanent damage to the cardiovascular system may be suspected.

With us at Jefferson Barracks, Missouri, an attempt was made to cull out these defectives before they were taken into the service. We were not wholly successful in that certain men, who were examined before we fully appreciated the condition and who apparently were normal, later were admitted to hospital with the characteristic symptoms. These men had developed the symptoms under the setting-up exercises and comparatively light military duty given them at this post. Certain men, thought by us to be border-line cases, given the benefit of the doubt and accepted, also later were admitted to the hospital.

Tachycardia is known to be produced by a variety of conditions. Hence at the final examination in the Examining Barracks by the two members of the special board, the tuberculosis and cardiovascular examiners, cases were sorted into several categories. Some were frankly tuberculosis and were at once rejected. Some were cases of exophthalmic goiter, of definite hyperthryoidism, of cirrhosis of the liver, chronic malaria with enlarged spleen, bronchial asthma, etc., and were at once rejected. There were, however, others which could not be so summarily dealt with. These were cases in which tachycardia or very labile pulse was found, and in whom no definite lesion of any kind could be discovered. These men were sent to the hospital for further observation and examination.

After careful examination the men were placed in squads and daily exercised with mild setting-up exercises under the charge of a non-commissioned officer who had been schooled in the drill. The exercises recommended by Lewis were used. His C^{15} and D^{30} were given, supplemented by hikes of varying distances, and periods of double-quick. Temperature readings and pulse rates were taken on all patients every three hours. Exercise was so timed that the 3 P.M. readings were taken from twenty minutes to half an hour after exercise. In this manner we studied over 400 cases referred from the heart and lung room in the Examining Barracks. Many of these proved to be simple excitement tachycardia and no record was kept of them. We studied carefully 315 cases and exercised 158 in hospital. In 297 the records were complete enough for later use.

Disposition of Cases at Examining Barracks

60 cases	(37 per cent)	diagnosed	hyperthyroidism.....	Rejected
47 "	(29 per cent)	"	pulmonary tuberculosis...	Rejected
52 "	(32 per cent)	"	irritable heart.....	Rejected
2 "	(1.2 per cent)	"	cirrhosis of the liver.....	Rejected
1 case	(.8 per cent)	"	bronchial asthma.....	Rejected

Disposition of Cases Observed in Hospital

40 cases	(29.6 per cent)	no lesion found, normal.....		Accepted
17 "	(12.6 per cent)	diagnosed	hyperthyroidism.....	Rejected
47 "	(34.8 per cent)	"	pulmonary tuberculosis..	Rejected
29 "	(21.5 per cent)	"	irritable heart.....	Rejected
2 "	(1.5 per cent)	"	cirrhosis of the liver.....	Rejected

It will be seen that cases of pulmonary tuberculosis and hyperthyroidism (including exophthalmic goiter) composed the greater proportion of the two groups. As a matter of fact the symptoms complained of by men are so similar in the cases of diseases named above and irritable heart that it is only after the most careful study that the cases can be separated into the proper group.

Our cases of irritable heart, the cardiovascular defective, fall into three groups:

(A). Strictly Cardiovascular.
   1. Following infectious disease. Chronic myocardial degeneration.
   2. Existing since childhood.
      (*a*) Associated with poor mentality.
      (*b*) Associated with good mentality.

(B). Some defect in endocrine secretion.
   1. Hyperthyroidism.
   2. Exophthalmic goiter.

(C). Associated with definite somatic lesions.
   1. Pulmonary tuberculosis.
   2. (Hodgkin's disease).
   3. Focal infections, chronic.
   4. Other diseases, cirrhosis of liver (hookworm) asthma, etc.

(A) The following case is typical of the first group, Subsection 1:

Case XXI. A. W. S., recruit aged twenty-seven, a farmer. His father died of cancer of the stomach. His mother is living, but is nervous. She has heart trouble and rheumatism. He has three half-brothers, one half-sister, children of same father. All are well. His mother was thirty-four years old when he was born. He went through the country school, but did not pass in all branches. Can read, write, spell, compute fractions. He left school at the age of sixteen, has worked on a farm since. Has worked hard and up to five years ago had never been ill. At that time he had rheumatism, evidently articular, which lasted for three months. He has never since that time been able to work hard. About one year ago he had "heat stroke." Since then he tires even more easily, has palpitation of the heart, gets dizzy and short of breath on slight exertion. The patient is tall, a healthy-looking and well-muscled man. Pulse sitting, 94, very labile. Hops 90 times on one foot and then is exhausted, dizzy. Pulse is 142, regular. He is breathless, has no pain. Two minutes later pulse 112. The apex beat is in the 5th i.s. 7.5 cm. from the m.s.l. Heart sounds are clear. The pulmonic second is accentuated. Diagnosis: irritable heart, caused by acute articular rheumatism resulting in myocardial weakness.

This case seems to have followed a severe attack of articular rheumatism, although the sunstroke was claimed to have made the man more easily exhausted. We have had several such cases. All occurred in farmer boys and all dated their symptoms from the sunstroke. If sunstroke, as claimed by some, is an infection, then the cases of effort syndrome following this cause must be classed as myocardial in character.

Cases belonging to the second subgroup of the first Group (A) are those which come strictly under the heading of cardiovascular defectives. In them no cause whatever can be discovered. They represent a class which has had a bad start in life. Tracing the family history reveals nervous instability on the part of one or both parents, alcoholism, or insanity. Often the mother is beyond the age of thirty when the boy was born. So many come from the farmer class that it would appear to be some environmental factor either affecting parents or child, or both, which produces tissues poor in resistance. These boys lack ambition. They do not think much about affairs in general. The work they do is desultory. Whenever they feel tired they stop for a while and rest. Such cases have had

little schooling. Some appear stupid from lack of opportunity, but the stupidity for the most part is that of mentality of a low order, and apparent underdevelopment of the brain. Such a case is the following:

CASE IX. H. C., recruit aged twenty-one years, a farmer, has a family history negative as to nervousness or any insanity. He had very little schooling, the history showing that he was not particularly bright. In the hospital here he appeared so subnormal mentally that he was sent to the psychiatry staff for examination. Nothing definite was found except slow cerebration. His complaint, dating back several years, was of breathlessness on exertion, exhaustion, and pain over heart. He was also nervous and unable to sleep at night. He stood the graded exercises poorly. He never drilled since entering the army February 25, 1918. Physical examination negative except for rapid heart. Apex beat within nipple line. Cannot hop 100 times. Pulse before exercise, 108; after exercise, 160. In two minutes still rapid, 130. Dizziness, exhaustion, and breathlessness complained of. Diagnosis: irritable heart. Recommended for Surgeon's Certificate of Disability.

The other class of case in this subgroup exhibits the same symptoms physically, but the mentality is above the average. It is no lack of opportunity for education in such cases illustrated above, but a real lack of ability to learn. This actually has no particular bearing upon the train of symptoms exhibited by these men. It only serves to group them into the two classes, in either one of which the same syndrome is brought out on slight exertion. The man with subnormal mentality necessarily never gets beyond a certain low scale in community life. His capabilities are necessarily so limited and his physical disability is so great that he has not the will to overcome his physical defects and force his brain to act. In the struggle for existence he can just keep himself above water. The man of the other class finds better living conditions and better pay provided he can obtain a position which supports him without the necessity of physical exertion. Such a case is the following:

CASE XXVI. L. C. B., recruit aged twenty-five years, is a clerk by occupation. His father has had nervous headaches for years and his mother's health is only fairly good. He was sick in bed for the greater part of his childhood because of nervousness, and missed a large part of his schooling.

He had no difficulty in learning when he was in school. Five years ago while at a show he became unconscious and remained in a stupor for three days. It was said to be nervous prostration. He has always suffered from headaches and has never been able to exercise on account of exhaustion, breathlessness, and headaches. He has been able to keep a position as city clerk where the work is very light and not very steady. He is not able to work every day. On examination he appears to be a robust young man. Lungs, heart, abdomen, show no abnormalities. Slight apical cardio-respiratory murmur is present. Sitting quietly, pulse 100. After hopping exercise, pulse 160. There was breathlessness, sweating hands, precordial pain, exhaustion, dizziness. Two minutes later pulse still fast, 130. Blood pressure normal. Diagnosis: irritable heart.

The second group, containing the subheadings hyperthyroidism and exophthalmic goiter, is too well known to need extended comment. The symptoms complained of by these men differ only in degree from those presented by the men with irritable heart. The important point to bear in mind is that these cases besides having tachycardia have also tremor of the extended fingers, lagging of the upper lids when looking quickly down, and often poor convergence at near vision. Besides, as we have shown elsewhere, the blood pressure in these cases is usually raised, whereas the blood pressure in the cases of irritable heart is normal or inclined to be slightly below normal. The blood pressure is raised in the hyperthyroidism-exophthalmic goiter group, and normal or below normal in the strictly irritable heart group. Diagnosis between these groups is not always easy nor is it always possible. One competent examiner will classify a case as one of irritable heart, an equally competent examiner will classify the same case as hyperthyroidism. The distinction appears to the writer to be valuable only in so far as the latter is a potential acute exophthalmic goiter. I do not believe there is any emotional shock violent enough to bring out Graves' disease in a normal man.

There is one difference which we discovered between the cases of true irritable heart (effort syndrome) and the cases of hyperthyroidism. That was the response to graded exercise. The former responded poorly. The latter were usually able to perform the setting-up exercises up to D^{30} with no subjective symptoms. The tachycardia was often the only sign of abnormal reaction. Occasionally the tremor of the hands was increased.

Group C. In this group are placed a number of diseases which cause in the victim symptoms so like the effort syndrome that only the most painstaking observation and examination will serve to make a correct diagnosis. Foremost among this group of diseases is pulmonary tuberculosis in the incipient stage. When patients have largely symptoms of the absorption of tuberculo-toxin without very definite physical findings, the problem of diagnosis is a difficult one. Our cases were always examined by at least two men and they were examined often where any doubt existed. The men were sent to the hospital because of persistent tachycardia, that being the objective finding which was most evident. They were placed in the group of cases under observation. The temperature, pulse, and respiration were taken every three hours and they were exercised by the drill instructor. By this means we were able to sort out the cases of tuberculosis from the other cases with tachycardia by observing the rise in temperature following exercise, and the development or increase of physical signs. The following case illustrates this point:

Case XV. L. L., recruit aged twenty-two years; complaint of loss of weight and exhaustion on slight exercise, with some dizziness and precordial pain. He had gradually developed these symptoms within six months. His family history was negative and his past history revealed no serious illnesses. He had always been healthy and able to work. On examination there were slight signs of infiltration at the left apex. Râles were variable. *X*-ray plates showed slight haziness at the left apex. There was no cough, no sputum. Even the slightest exercise caused him great distress and the temperature taken from twenty to thirty minutes after the exercise always showed a rise. The morning temperature was subnormal. Frequent examinations, the rapid temperature following exercise, and his exceedingly poor response to exercise led us to the diagnosis of incipient pulmonary tuberculosis. His exercise response was far more severe than any of the cases of irritable heart.

I feel sure that hookworm disease and early Hodgkin's disease would show the same effort syndrome. I have no case histories to prove my contention. I have only recollection of symptoms complained of in patients seen in civilian practice. Uncinariasis is easily diagnosed. Early Hodgkin's disease is not so easily detected.

Chronic focal infections also may show typical effort syndrome.

I have observed no cases in my studies, but I agree with those who make this assertion. I have not seen the removal of tonsils or the opening of nasal sinuses or the cleaning of apical tooth abscesses cure cases which had the effort syndrome, although I have no doubt that such cases do occur and such pathological conditions should always be kept in mind so that gross errors in diagnosis are avoided. I have seen bronchial asthma, cirrhosis of the liver, and chronic malaria in patients who had effort syndrome and tachycardia. These patients were much improved under treatment. Those with the last-named disease went back to duty.

Etiology. We do not know why certain healthy, even robust-looking men have this strange inability to respond as normal persons do to a slight amount of physical exertion. They are always in the condition of a normal man just convalescing from a severe illness. No wonder that they lack ambition to overcome obstacles, and are passed in the race of life. In the history of the cardiovascular defective certain points may be emphasized. The first is the parental history. These men do not have a fair start. One or both parents suffered from nervousness, chronic headaches, insanity, or were alcoholic in *55* per cent of the cases. Practically all the men dated their symptoms into childhood. "As long as I can remember" was a frequent response to the question, "How long have you had these symptoms?" In only *50* per cent of my cases was there a definite time set which followed some infectious disease. The other *50* per cent could set no time of onset, nor could they say that infectious disease had any relation to the symptoms. The fact that so many of these defectives come from a neurotic parentage and are brought up in an environment surcharged with bodily complaints renders them introspective of their small ailments. Eventually their mental states so dominate the somatic functions that trivial sensations are magnified to an extent which causes them acute suffering. Should this take the form of palpitation of the heart, sensible to them, and should some doctor tell them they have heart disease and treat them for it, the cases become practically helpless hypochondriacs. The following is illustrative of this group:

Case XXX. F. C. J., recruit aged twenty-five years, was a big, healthy fellow, but always had a worried look. He entered the army at this post July 11, 1918, admitted to the hospital July 16. His mother was neurotic, a

fussy woman; his father was well. Several brothers and sisters were all well. As a child his mother said he was always nervous, never could play with the other children as he became easily exhausted. He was evidently nagged during his youth. When he was old enough to work he was taken away from one position after another as soon as he made any complaint. Finally, about four years ago, his mother took him to a doctor, who told him he had serious heart disease and treated him for it up to the time he was drafted into the army. He was married and was supported by his wife and mother. He could not do any work. He complained of inability to perform even the slightest exercise. He was obsessed with the idea that he had serious heart trouble, his mother and wife abetting him in this belief. On slight exertion, heart pounded, he had precordial pain, dizziness, headache, breathlessness, and exhaustion. On physical examination he was tall, well built, and a strong-looking man. The pulse was always rapid. The heart was slightly enlarged. There was a soft, short systolic murmur at the apex not considered to be organic. The lungs were negative. The blood pressure was 116–80. Exercise response was poor. There was rapid pulse, pounding heart, and anxious expression. The vasomotor instability was marked. Diagnosis: irritable heart, hypochondriasis.

Frequently in the histories of these cardiovascular defectives there will be fainting spells, attacks of dizziness, when everything gets black, or there will be convulsive seizures and unconscious periods lasting for hours or days. Attacks of nervous prostration in children are not uncommon. Such abnormal conditions can only occur on a marked neuropathic basis. The cases which date their symptoms from some infectious disease have not given such histories. They complain only of the symptoms which follow exertion and which they are certain were not present previous to the illness. In these cases one may feel reasonably sure that the myocardium has been permanently damaged. Dilatation of the heart following slight exertion will account for all the symptoms of the effort syndrome.

Where no cause can be assigned we are forced back upon the term "constitutional inferiority," which explains nothing. It simply states a fact with which all are familiar.

Graded Exercise. Graded setting-up exercises were begun with the idea of hardening the men so that they could do full duty. It was thought that a certain number of men with the effort syndrome could be gradually strengthened. Before the cases were fully recog-

nized at the Examining Barracks some men were accepted who had mild symptoms with slight tachycardia at rest. These men were put out at the usual setting-up exercises. Some fainted, some grew so dizzy that they had to be excused, some managed to get through a day's exercise, but were exhausted and bed-ridden for the next day or two. Hence it was felt that a more gradual break-away from their sedentary civilian lives would render these men less liable to break down under violent exercise. In this we were disappointed. In no case of true effort syndrome was there any betterment even after days of the slightest exercise. Any attempt to go from very light to a light exercise brought on symptoms more violent than before. On the other hand, there were cases diagnosed irritable heart at the Examining Barracks who were accepted for Limited Service. Two months later at the examination for demobilization many of these men had normal cardiovascular response to exercise. In every case where the condition had apparently cleared there were absolutely no symptoms complained of at any time in the man's life except the pounding of the heart following violent exertion in men who were unaccustomed to exercise. They were clerks or others who led sedentary lives. On the contrary, the cases which still revealed the effort syndrome were those who had complained of precordial pain or dizziness, with the pounding heart after exercise and previous to their induction into service. These men without exception stated that they had not been able to stand the light drill and had been working the past two months as clerks. This lends weight to the point that in the history of the man there *must* be one or more of the cardinal symptoms of the syndrome. The tachycardia alone is not sufficient for diagnosis. The pulse may remain rapid longer than two minutes after the usual test exercise of hopping 100 times on one foot. There may even be great exhaustion present, but if there have been no symptoms which careful inquiry has elicited, one is not justified in diagnosing the case irritable heart.

The temperature of every patient was taken twenty minutes after exercise. The cases of pulmonary tuberculosis could be picked out by the temperature reaction. All the men exercised were those upon whom a definite diagnosis had not been made. It was found that cases could be sorted into groups according to their response

to exercise. For example, the cases of suspected hyperthyroidism responded best to exercise. The pulse rate was not so high, there was no rise of temperature, and symptoms were not so severe as a rule. Further, they often were able to increase exercise without discomfort. The cases of effort syndrome showed no improvement under exercise. They often grew worse and had to be excused. The temperature was not raised in these men. The cases of suspected pulmonary tuberculosis usually responded badly to exercise. They became easily exhausted, showed marked breathlessness. The temperature was always raised from 10 to 30 after exercise and there were frequently râles heard over one or both apices where none had been heard before. Graded exercise, therefore, is not only of therapeutic value, but it becomes of real diagnostic value under certain circumstances. Further, in the cases of effort syndrome where the symptoms dated definitely from some serious illness, often ten to fifteen years previously, there was frequently demonstrable an actual displacement of the apex beat to the left following the exercise. This could have but one meaning and hence was interpreted as dilatation of the left side of the heart.

Prognosis. As has been stated, it has not been possible for us to benefit these cases by graded exercise. After some experience with the cardiovascular defectives we rejected them after studying them in hospital, in order to be sure we were making no mistakes in diagnosis. Those with marked psychoneurotic state we consider to be hopeless spongers on their families or on the communities in which they live. For other cases who have been making a living at farming or clerking, we see no reason to predict any bad fate. As long as they recognize their limitations and live always within them, they should have no difficulty in keeping well and free from distressing symptoms, chiefly palpitation and precordial pain.

A CASE OF AYERZA'S DISEASE:

CHRONIC CYANOSIS, DYSPNEA, AND ERYTHREMIA, ASSOCIATED WITH SYPHILITIC ARTERIOSCLEROSIS OF THE PULMONARY ARTERIES

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THE discovery by Vaquez, in 1892, of the syndrome of chronic cyanosis, persistent polycythemia, and enlargement of liver and spleen, in the absence of organic heart involvement, and Osler's service later in calling the attention of the medical profession to this new complex, established a definite place for it in nosology as Vaquez's disease, Osler's disease, Osler-Vaquez disease, erythremia, primary polycythemia, splenomegalic polycythemia, polycythemia with chronic cyanosis, myelopathic polycythemia, cryptogenic polycythemia, erythrocytosis megalosplenica, etc. Lucas (1) collected 149 undoubted and 30 questionable cases from the literature. Since his paper the number reported has increased to over 200. Lucas, in his summary, came to the conclusion that, in the light of the present knowledge of the disease, it was difficult to establish a hard-and-fast line between cases of polycythemia, probably secondary in form but of obscure origin, on the one hand, and unquestionable cases of primary polycythemia or erythremia on the other. The 23 reported autopsies had thrown but little light on this question.

Since Lucas' paper the question as to the primary or secondary nature of the Osler-Vaquez syndrome has received more attention, and there is an increasing number of cases in which the syndrome has been found associated with other conditions in such a way as to make it certain that the symptom-complex was purely secondary. The separation of a primary polycythemia from a secondary erythrocytosis has become more difficult, and the question may well be asked if a primary Osler-Vaquez disease exists. The uncertainty

attending this question has led recent writers to split up the Osler-Vaquez disease into a number of groups. The fact that cases are reported under such titles, or are classed as "Polycythemia without splenomegaly," "Polycythemia without cyanosis," the "frustrate form," congenital form, cardiac form, "Geisbock's disease," "Blumenthal's disease," etc., reveals the confusion attending the effort to fix the symptom-complex as a distinct morbid entity. Similarly the attempts to separate forms upon a basis of the number of red cells, state of the bone-marrow, etc., are evidence of the difficulty in giving the syndrome a fixed position in nosology.

Does a primary erythremia exist? The writer believes not, certainly not in cases showing chronic cyanosis and dyspnea. Why should a case of pure or absolute polyglobulism have either cyanosis or dyspnea? On the other hand, there is every reason why a case of chronic cyanosis and dyspnea should develop a chronic erythremia. It is most probable that all erythremias associated with cyanosis and dyspnea (with a theoretical exception of a neoplastic overformation of red cells, yet to be definitely shown to exist) are *compensatory* in nature (secondary to pulmonary sclerosis, emphysema, congenital heart lesions, chronic pulmonary diseases leading to insufficient oxygenation, increased resistance of the red cells with lessened oxygen-carrying capacity, etc.).

With this point stated, the writer presents a unique case of Osler-Vaquez disease, which was under clinical observation for five years, with full autopsy and microscopic findings, in which the Vaquez syndrome of chronic cyanosis, persistent high erythremia, enlargement of liver and spleen, and hyperplasia of bone-marrow, are shown to be secondary to syphilitic disease of the pulmonary arteries (Ayerza's disease).

CASE. L. H., American, forty-three (?) years of age, laborer, was admitted to the Medical Clinic (Dr. George Dock) of the University Hospital, Ann Arbor, January 17, 1907, and was presented in the Clinic on the following day. His chief complaints at that time were difficult breathing, palpitation, blueness of skin and lips, general weakness, dropsy, and frontal and occipital headaches.

His family history, as far as known to him, was negative. His father was living; his mother had recently had an amputation of right tibia for thyroid metastasis. He was unmarried. He denied venereal disease, and

claimed to drink and smoke but rarely. His health had been good up to about thirty years of age, when he began to have asthmatic attacks at night. These increased in severity and frequency. At thirty-six he had a sudden attack of apnea, and was unconscious for several minutes. From this time on he had more frequent and severe asthmatic attacks, at irregular intervals, usually at night. Four years before entrance to the hospital he first noticed blueness and swelling of his face, hands, and feet. He was told by a physician that he had "heart trouble," and under medical treatment his symptoms improved; the cyanosis disappeared and did not return until September, 1906. From this time on attacks of cyanosis, palpitation, and dyspnea became more frequent and severe, with severe frontal headaches, frequent dizziness, prominence of eyes, feeling of thoracic constriction, particularly when lying down. Pressure upon sternum produced a sensation of "smothering." He had no dysphagia, and no marked gastrointestinal disturbances.

Physical examinations by Drs. Dock and Smithies showed a man of medium build, with thin panniculus, with marked cyanosis over face and neck; hands and feet were moderately blue; color deepened when patient stood or let his arms hang down. When lying down face and neck became slaty blue, the cyanosis decreasing after several moments. Exercise and excitement increased the cyanosis. Palate and tongue were deep purple; eyes prominent, especially the right. Conjunctivæ suffused, especially on right. The pupils were of moderate size, equal and active. The external jugulars were prominent, dilated, and filled from adove. There was moderate pulsation of the carotids. The thyroid was negative; no tracheal tug. Over the trunk the skin had a bluish cast. The thorax moved *en cuirasse;* respirations were shallow, not increased when resting, but rapidly increasing on slight exertion. Heart beat faintly seen in 5 i. c. s., inside the nipple. Heart rate not increased. No arrhythmia. Palpation of lungs negative. Percussion showed good resonance over lungs, low liver dullness, an abnormal area of dullness beneath the upper portion of sternum, and an atypically situated precordial outline. Splenic dullness barely made out to edge of ribs. Auscultation of lungs showed diminished vesicular over entire right side above fifth rib; below this inspiration was sharp and blowing, expiration soft and prolonged, with few piping râles. On the left side there was bronchovesicular breathing to the second rib, with increased vesicular below, with more numerous râles. Spoken and whispered voice were negative.

Auscultation of heart revealed faint sounds heard with difficulty. The first sound at apex was soft and impure; the pulmonic second moderately accentuated. Over base of heart sounds could barely be heard.

The radial pulse was slow, moderately full, fuller on left than on right. Radial arteries moderately sclerotic. The blood pressure varied on the two sides; on the left systolic was 156 mm. Hg, diastolic 109 mm.; on the right the systolic was 146, the diastolic 98 mm. (Erlanger apparatus, 12 cm. cuff).

The abdomen was somewhat distended in region of umbilicus. Lower border of liver dullness low. The liver was felt with difficulty at the end of inspiration. Splenic dullness to edge of ribs. Spleen was not palpable. No palpable mass in abdomen. Lymph nodes not enlarged.

Ophthalmologist's (Dr. W. R. Parker) examination of eyes showed a moderated conjunctival injection; marked venous congestion of retina, with edema of macular region. No hemorrhages.

Left nasal fossa was partly occluded. Examination of larynx negative.

When presented in the Medical Clinic, January 18, 1907, the red blood cell count was found to be 6,450,000, white cells 6500, and hemoglobin 100 per cent. The blood was deep red in color, flowed slowly. The red cells were normal in appearance; no nucleated forms were seen, and the differential white count was negative. Urine contained a moderate amount of albumin, and many small granular casts and cylindroids. A tentative diagnosis of "Osler-Vaquez disease" was made by Dr. Dock at this time.

Later fluoroscopic examination showed a vaguely outlined, diffuse, non-pulsating shadow above the heart, especially dense about the root of the lungs and great vessels, extending up into the neck. Heart downwards and inwards. Diaphragm low on both sides, especially so on right side.

A radiogram confirmed the fluoroscopic findings, "a mass, almost as dense as the heart, filling in the mediastinum. No definite lines of pulsation can be seen. Tumor appears to occupy both mediastinal spaces, lying in close approximation to heart, lungs, and adnexa. Points of greater or less opacity can be seen throughout the lungs, the infiltration being more marked on the left than on the right."

Course of Disease. The patient at first improved somewhat under treatment, was able to go about the hospital, his cyanosis, erythremia, and dyspnea varying in degree with conditions. About three months after entrance, while walking in the hall, he had a sudden sense of pressure in upper thorax, "felt as if he were being choked," could not breathe or speak, fell to the floor and became unconscious. When placed in bed was cyanotic and markedly dyspneic, and complained of pains in thorax. Respiratory sounds were very weak with numerous piping râles; heart sounds very weak, rate 129; systolic pressure 106, diastolic 55.

This attack was followed by a period of increasingly frequent attacks of extreme cyanosis, with more or less pronounced erythremia, marked

dyspnea, associated with unconsciousness, headaches, gastrointestinal pain, and albuminuria. He was constantly cyanotic, but during the two years he was in the hospital had about seventeen attacks of extreme cyanosis ("black"), with extreme dyspnea, feeling of suffocation, precordial distress and palpitation (angina hypercyanotica), these attacks lasting for a few minutes or for several hours. During the attacks the heart rate was accelerated, going from 60 to 130. The peripheral vessels were injected, but there were no positive venous pulsations. During the attacks there was almost complete absence of breath sounds, with few high-pitched musical râles. Heart sounds became very faint. The eyegrounds always showed extreme engorgement and edema. There was no bleeding, except occasionally from nose. Enlargement of the spleen was first positively determined October 21, 1907, when it could be palpated below the edge of the ribs.

The *erythremia*, which had been noted on entrance, persisted, varying greatly, usually in proportion to the severity of the attacks of cyanosis. In over 100 blood counts taken during the 605 days in hospital, the red blood cell count only twice fell below 6,000,000, the lowest count being 5,040,000 on March 25, 1907, and the highest 9,500,000 on May 8, 1908. The average of these counts was over 8,000,000 per c.mm. Blood taken from different parts of the body showed some variation in the number of red cells. The hemoglobin was always above 100 per cent, frequently as high as 156 per cent (Miescher); with prolonged paroxysms of cyanosis and red blood cell counts of 8,000,000 per c.mm. the average hemoglobin reading was 132 per cent. The white cell count ran within normal limits, 6–10,000, and the differential white count showed little variation; at times a slight increase in eosinophiles and lymphocytes, and occasionally a few myelocytes after one of the acute attacks. Nucleated reds were occasionally noted. With the red cell count 7,400,000, specific gravity of blood was estimated at 1.062; coagulation time shortened; viscosity increased.

The patient remained in the hospital 605 days, being discharged September 12, 1908. At the time of discharge he was still showing an increase in the severity of his attacks of cyanosis, dyspnea, headaches, visual disturbances (diplopia, "turning black"), gastrointestinal symptoms (loss of appetite, intense paroxysmal pains in epigastrium radiating to lower abdomen, constipation alternating with diarrhea). His albuminuria had increased. Stools were negative. He had no dysphagia or vomiting. Temperature was never raised. The last radiograms seemed to show a gradual extension of the mediastinal mass.

Dr. Dock inclined to a diagnosis of Osler-Vaquez disease with albuminuria and chronic pericarditis; Dr. Smithies to a diagnosis of polycythemia

with mediastinal tumor. The case was reported by the latter, as Case I, in an article on "Clinical Aspects of Tumors of the Mediastinum." (2) In this article, Dr. Smithies summarized the case as follows: "The case presents many of the findings of the condition of chronic cyanosis with erythremia described by Vaquez, Osler, et al. The spleen, however, is not enlarged, and the mediastinal tumor appears to be a discoverable cause for the symptoms, which is unusual or not yet reported for cases of true cyanotic polycythemia, Vaquez-Osler malady. It is not quite determined that the two conditions do not exist, but in view of the rather marked variations in the cyanosis and the red cell count, it is probable that much of the polycythemia is due to extensive pressure in the thorax on the great vessels. The changes in spleen and bone-marrow might come on later and give a characteristic picture of erythremia vera."

After leaving the hospital in 1908, the patient became a pop-corn peddler in Ann Arbor, and was seen at intervals by members of the Staff of Internal Medicine. He was still subject to attacks of cyanosis and dyspnea; but was for some time more comfortable than he had been the previous two years. He was able to work at his pop-corn business about half the time.

On April 28, 1910, his blood count was again made in the Clinic of Internal Medicine (Dr. A. W. Hewlett). The red cell count was 7,200,000, white cells 10,500, and hemoglobin 120 per cent. He was first examined by Dr. Hewlett on the next day. He found his heart enormously dilated, the lower portion of the chest retracted and immobile. Abdomen was prominent, but there was no ascites. Spleen was just palpable. Lungs showed signs of emphysema, but little bronchitis. Legs were moderately edematous. The spectroscopic examination of his fresh blood, which was dark and thick, gave the characteristic band of oxyhemoglobin. Urine showed trace of albumin and few granular casts. He appeared at intervals for examination and advice, his condition remaining about the same.

In the *Transactions of the American Ophthalmological Society*, 1910, his case was again reported, this time from an ophthalmological standpoint, by Drs. Parker and Slocum, of the University Clinic of Ophthalmology.

By this time the diagnosis of a mediastinal tumor had been completely abandoned, and the case was regarded as an uncomplicated one of "Chronic Cyanosis with Polycythemia (Osler-Vaquez Disease)." Parker and Slocum give in their article (Case I) a detailed description of the retinal appearances of intense engorgement and edema. They noted the presence of a small venous aneurysm, which later was found to have ruptured. A second retinal hemorrhage was also seen.

When patient was seen, December 2, 1910, his cyanosis was greatly increased; his hands were black.

On January 31, 1911, Dr. Hewlett found the spleen fairly easily palpable and "purpuric" spots about his joints and over his legs, some as large as a dime, and elevated. During the winter he had a very severe attack, and vomited black particles.

Readmitted to the hospital on October 24, 1911, his condition obliging him to give up work. At this time he gave his age as fifty-two. His chief complaint was still dyspnea, weakness, and cyanosis. He still denied venereal disease and alcoholism. His symptoms were about the same as when last seen. He had not lost weight; had had no blood in stools or sputum. Vision is blurred at times; and he has headaches accompanied by dizziness and nausea. Claims to sleep poorly at night; but is drowsy during the day. Sleeps between examinations. Has no thoracic pain.

Physical examination (Drs. Hewlett and Van Zwaluwenburg) showed less cyanosis than in previous admissions. Had firm, hard edema over thighs and legs, not much over back; face was puffy. Conjunctival vessels were enormously engorged; many venules were blue-black. Veins of neck were full until patient was almost upright, when they collapsed. Thorax moved poorly; there was inspiratory retraction all the way round at level of diaphragm. Abdomen was full, flat above and bulging in the flanks. Abdominal breathing marked. Percussion showed an enormously enlarged heart. Liver was a hand's breadth below the level of the ribs, reaching nearly to navel and confluent on left with splenic dullness. Lungs were nowhere very resonant; the lower borders moved slightly, but symmetrically. No localized areas of diminished resonance over front or back. Tactile fremitus was negative. Breath sounds all over the lungs were feeble, vesicular, almost inaudible over bases and back. Numerous crackling râles were present over the upper portion, large dry ones below, somewhat more abundant on right. The whole left upper portion more silent than on right. No localized voice changes. The first sound at apex was dull and distant, almost replaced by a systolic murmur; second sound poorly heard, although easily felt. The murmur waned and waxed to another maximum in the fifth i. c. s., about 2 fingerbreadths to left of sternum. It was poorly transmitted to axillæ, and not heard in back. The second sound in the tricuspid area was relatively loud. At base both sounds were distant; valvular areas could not be accurately localized; systolic murmur from below was only occasionally audible at base. No diastolic murmur. The radial pulse was small, soft, quick, and frequent. Hands were cold and moist. The liver margin was felt as a firm semi-elastic mass without a distinct edge. The spleen was just palpable in the anterior axillary line in the left hypochondrium. Otherwise belly was tympanitic. No fluid wave. Ophthalmological examination showed similar retinal engorgement and edema as before, only more marked.

Erythremia was variable as before, 7,200,000–8,760,000. The white cells ranged 7–10,600; the proportionate count was almost normal, the polynuclears being slightly increased. No nucleated forms and no myelocytes were found at this time.

The patient's condition quickly grew worse, increasing dyspnea and cyanosis, weakness, somnolence, nausea, "purpura," and finally bloody stools, blood-streaked sputum, delirium, intense cyanosis ("black"), general collapse, leading to his death on November 14, 1911.

Clinical Diagnosis. Polyglobulism, Emphysema. Cardiac hypertrophy and dilatation. Chronic passive congestion. Cardiac cirrhosis. Hemorrhage from hemorrhoids. Nephritis (?) (Dr. Hewlett).

The autopsy was performed a few hours after death.

Autopsy Protocol (Dr. Warthin). Male body, of medium frame, 172 cm. long; abdomen distended; umbilicus everted; broad epigastric angle; precordium prominent. Skin of entire body markedly cyanotic; where least cyanotic, on the upper portions of body it is yellowish blue. Hypostasis is extreme, particularly on legs. Genitals very cyanotic and slightly edematous. Numerous angiectatic warts over back, black in color. Over legs numerous circumscribed angiectatic vessels, forming blue-black spots size of pin-head to dime. No hemorrhages in skin. Skin over legs thickened and scaly. All superficial veins markedly injected. Mucous membranes intensely cyanotic. Scleræ yellowish. Musculature fair. Fair amount of panniculus. Marked edema over legs, moderate over trunk and upper portion of body. Rigor mortis present throughout. Palpation of abdomen negative. Liver and spleen could not be felt.

Head: Skull-cap moderately thick, but almost as thin as paper in left temporal region. Meningeal grooves deeply eroded, particularly that of the left middle meningeal artery. Inner table shows marked erosion. In the right temporal region there is a sharp, spine-like exostosis projecting 1 cm. from the inner table. Dural tension increased. Dura adherent all over convexity, thickened, and very tough. Adhesions between dura and arachnoid. Longitudinal sinus contains a small red clot; the veins opening into it have markedly thickened walls. Basal meninges thickened. Arachnoid over convexity thickened, and shows hyaline patches. Pial vessels enormously distended. Pacchionian bodies extremely small. Carotids and basal vessels show no sclerosis. Cerebrum intensely congested and edematous. Ventricles moderately dilated. Chorioid plexus markedly congested. Pineal gland very small. Cerebellum intensely congested and edematous. Hypophysis very small.

Spinal cord presents meningeal thickening, congestion and edema.

Main Incision: Panniculus very moist, light orange color. All blood

vessels engorged with dark fluid blood. Muscles are light brownish-red, soft, and tear easily. No free gas in peritoneal cavity, and only a small amount of clear fluid (150 c.c.). Omentum below umbilicus, moderately fat, its vessels congested. Lower border of liver reaches to umbilicus in median line; in right nipple line it is a hand's breadth below edge of ribs. Spleen is large, its lower pole below edge of ribs. Stomach lying vertically, moderately distended with gas. Curious sweetish smell in abdominal cavity. Diaphragm in lower border of sixth rib on the right, in sixth i. c. s. on the left.

Sternum osteoporotic, marrow hyperplastic. No free gas in pleural cavities. Small amount of clear fluid (100 c.c.) in each cavity. Old adhesions over right apex; otherwise pleuræ are free. Lungs nearly meet in upper portion of mediastinum; their free edges show extreme emphysema. Mediastinal fat fairly abundant, very red in color. No remains of thymic tissue seen.

Heart: Of enormous size, lying almost transversely; the greater part of the right heart lies to the right of the median line, the apex in sixth i. c. s., half-way between nipple and anterior axillary lines. Apex is rounded, blunt, with no point. Pericardial sac greatly distended; no pericardial adhesions; fluid about 80 c.c., clear. All chambers of heart greatly dilated, particularly the right heart, the dilated right auricle making up one-third of the heart bulk. Right border of right auricle reaches to the right parasternal line. On cutting the inferior vena cava there is a gush of very dark fluid blood containing small jelly clots. Left and right ventricles about equally dilated; both auricles extremely dilated, the right one in a remarkable degree; the muscle fibers of its wall widely separated. The enlargement of the heart is due chiefly to dilatation; when emptied of blood its measurements are 18 x 13 x 7.5 cm., its weight 790 gm. On the table the heart flattens into a soft round disk. The subepicardial fat is increased, orange-red in color. Irregular tendinous spot over anterior wall of right ventricle. Firm thrombus in right auricular appendage. Mitral orifice admits five fingers, slight roughening and thickening of proximal edges, but no organic insufficiency or stenosis. Aortic orifice barely admits thumb; flaps negative. Tricuspid orifice greatly dilated, admitting whole hand; flaps negative. Pulmonary orifice admits three fingers, two and a half times as large as the aortic opening. Calcareous plaque in wall of pulmonary conus. Pulmonary artery enormously dilated; its wall markedly thickened, and its intima showing a condition of advanced atherosclerosis. Coronaries extremely dilated, presenting patches of sclerosis. Auricular ventricular septum intact; foramen ovale closed; no anomaly. Aorta is of medium size; its intima shows moderate sclerosis rather linear in type, with some early atheroma.

FIG. 1. MAIN BRANCH OF PULMONARY ARTERY, SHOWING EXTENSIVE ATHEROSCLEROSIS AND MESARTERITIS.

FIG. 2. MEDIUM-SIZED BRANCH OF PULMONARY ARTERY, AT EDGE OF SCLEROTIC PATCH.

FIG. 3. MEDIA OF MAIN BRANCH OF PULMONARY ARTERY, SHOWING AREA OF PLASMA-CELL AND LYMPHOCYTE INFILTRATION OF THE MEDIA (SYPHILITIC MESARTERITIS).

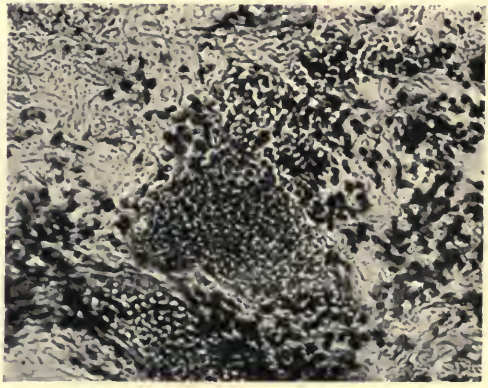

FIG. 4. PLASMA CELL INFILTRATION ABOUT ONE OF THE VASA VASORUM OF THE MAIN PULMONARY ARTERY.

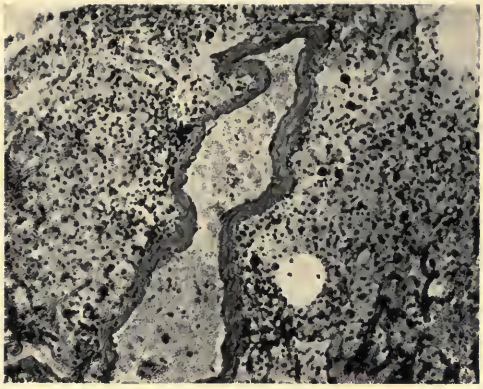

Fig. 5. Dilated and Sclerotic Smaller Pulmonary Arterial Branch.

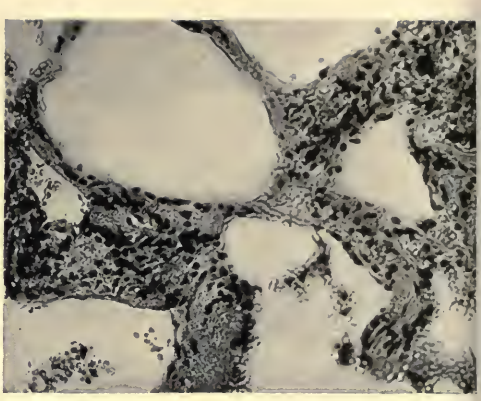

Fig. 6. Air Containing Portion of Lung, with Thick Alveolar Walls, and Some Emphysematous Alveoli.

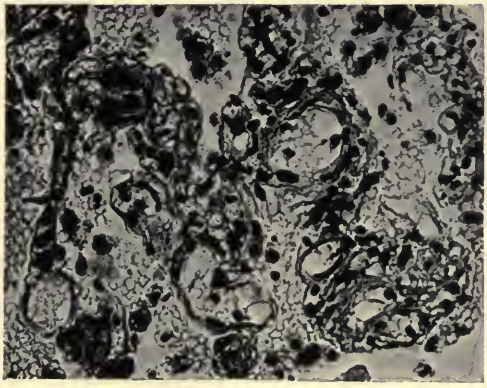

Fig. 7. Atelectatic Fibroid Area of Lung, Showing the Thickened Sinusoidal Capillaries.

Lungs: Right and left lungs weigh 625 and 675 gm. respectively. Both are very voluminous, with markedly emphysematous borders. Moderate anthracosis. Both show extreme congestion and edema. Airless areas alternate with emphysematous. All the branches of the pulmonary arteries are markedly dilated, and present an extreme condition of sclerosis and atheroma, even to the terminal branches. Lower lobes show patches of pneumonic or hemorrhagic consolidation. In the larger main branches of the pulmonary arteries the thickened intima shows porcelain-like areas, with irregular cracks and thinnings of the wall, as in syphilitic aortitis. Pulmonary veins enormously distended; their walls relatively thickened. Bronchial nodes pigmented, much congested and edematous.

Mouth and Neck Organs: Mucous membranes of mouth, pharynx, epiglottis, larynx, and trachea show extreme congestion. Thyroid is small, with small amount of colloid. The parathyroids are of normal size, and very deep red. The cervical fat has the appearance of embryonic fat. Cervical lymph nodes extremely congested.

Spleen: Free, no adhesions. Greatly enlarged before removal; much smaller after removal and bleeding; measures then 13 x 9 x 6.5 cm., and weighs 330 gm. Firm, does not flatten on pressure. Capsule thickened, with small hyaline patches. Cut surface shagreened, deep bluish-brown-red. Stroma increased; follicles not easily seen.

Adrenals: Normal in size and shape. On section show intense congestion. Medulla of right one in advanced post-mortem change.

Kidneys: Left and right measure 13.5 x 8 x 5.25 and 13 x 7.5 x 4.5 cm. respectively, and weigh 300 and 200 gm. They present similar appearances. Fatty capsules are abundant, reddish orange, resembling fetal fat in color and appearance. Fibrous capsules strip easily. Cortical surface smooth, deep purple-red, with small areas of parenchymatous degeneration in cortex. Cortex atrophic. Cut surfaces nearly uniform in color; outlines of structure cannot be made out.

Intestines: Contain a thin, soup-like, bile-stained material. No fresh blood seen. Mucosa shows extreme congestion and edema. Appendix surrounded by old adhesions. Bile passages patent. No hemorrhoids. No bleeding in rectum.

Stomach: Contains a plum-colored mucus containing some food remains. No fresh blood. Mucosa tremendously congested; chronic stasis catarrh. Pylorus thickened, firm, slight stenosis. No erosions or ulcers.

Pancreas: Large, firm, body ends abruptly without tail. Color very dark. On section shows marked congestion; lobules large with increase of interlobular connective tissue. Vessels dilated and show slight sclerosis.

Liver: Much enlarged, shows markings of ribs. After removal and bleed-

ing measures 25 x 19 x 8 cm. and weighs 2000 gm. Capsule shows some thickening, particularly around ligaments. Lower border rather rounded. Consistence soft. On section bleeds freely. Marked "nutmeg liver." Vessels all greatly dilated. Stroma increased in patches beneath cortex. Gall bladder greatly distended. Contains thin brownish fluid.

Lymph Nodes: Mesenteric and retroperitoneal lymph nodes extremely congested, edematous, and very soft. Few atrophic hemolymph nodes, brown in color.

Prostate: Negative, except for intense congestion.

Testes: Marked congestion and edema.

Bone-marrow: Hyperplastic red marrow in sternum and ribs. In tibiæ fatty marrow.

Microscopic Findings. Brain: Extreme dilatation and congestion of all vessels, particularly of the meningeal and pial. Diffuse thickening of the inner meninges. Chronic leptomeningitis.

Cord: Marked congestion of all vessels, particularly of the meningeal. Diffuse thickening of the meninges.

Heart: Hypertrophy. Brown atrophy. Fibroid patches. Healed syphilitic myocarditis. No active areas.

Aorta: Advanced atherosclerosis with patches of active syphilitic mesaortitis.

Lungs: Extreme chronic passive congestion with numerous pigmented phagocytes, "brown induration." Main branch of pulmonary artery shows extreme atherosclerosis of the intima and inner half of the media with active patches of syphilitic mesarteritis, and plasma-cell infiltrations around some of the vasa vasorum. The intrapulmonary branches of the pulmonary artery show extreme dilatation with marked atherosclerosis of the intima and inner one-half to one-third of the media. In the branches of the second and third degree a few small plasma-cell infiltrations around the vasa vasorum are found, but the majority of these branches show no active syphilitic lesions. The smaller branches of the pulmonary vessels are extremely dilated, with thick hyaline walls showing no active process. The alveolar capillaries are greatly dilated; have thickened hyaline walls. In some areas the thickened alveolar walls appear almost like that of a cavernous angioma. In other areas the alveolar walls are atrophic, hyaline, and the capillaries almost obliterated, the alveolar partitions extending into the dilated infundibula as stiff hyaline septa. In some portions of the lung, the circulation is completely shut off and the lung is fibroid and collapsed. Hemorrhages in all stages are found everywhere throughout the lung. There is marked edema, and great numbers of pigmented phagocytes. Emphysematous areas are scattered through the indurated portions. The

hyaline indurated portions of the lung are particularly the seat of anthracotic deposits. The bronchi and bronchioles are dilated and show catarrhal bronchitis. Small patches of early broncho-pneumonia are also found, particularly in the lower lobes. The pulmonary veins are extremely dilated, and show hyaline thickened walls without atheromatous changes.

Thyroid: Moderate amount of colloid. Extreme congestion of vessels.

Tongue: Numerous encapsulated trichinæ. No reaction about these.

Spleen: Extreme dilatation of blood spaces and blood vessels, many portions resembling an angioma simplex rather than spleen. The lymphoid tissue of the pulp is atrophic. Follicles are of fair size, arterioles sclerotic. The larger arteries show hyaline thickening of their walls.

Adrenals: Marked congestion, particularly in the reticular zone and medulla. Extensive medullary hemorrhage. Cortex shows extreme lipoidosis. Several small plasma-cell infiltrations in the reticular zone.

Kidneys: Extreme congestion, involving both arteries and veins. Marked hypertrophy of glomeruli, many being two to three times normal size, due to increase in size of capillary tufts. Majority of Bowman's capsules are thickened, and there is a diffuse increase of connective tissue, with many scarred glomeruli, with definite areas of chronic parenchymatous nephritis. Vessels all sclerotic. Slight cloudy swelling of convoluted tubules.

Stomach: Chronic catarrhal gastritis. Extreme congestion of both arteries and veins. In the stomach wall there are numerous areas of plasma-cell infiltration and localized induration, probably syphilitic.

Intestines: Extreme congestion of arteries and veins. Slight catarrh.

Appendix: Extreme congestion of arteries and veins. Thickening of sub-mucosa.

Pancreas: Extreme congestion of arteries and veins. Thickening of vessel walls. Fatty atrophy. Areas of marked intralobular interstitial pancreatitis with some active plasma-cell infiltrations. Many islands of Langerhans are very large and show marked dilatation of the vessels.

Liver: Extreme nutmeg liver. Atrophy and necrosis of cells of central and intermediate zones. Dilatation of all vessels with atrophy and slight cloudy swelling of liver cells. Slight fatty degeneration, particularly of the central zones of the lobules. Capsule is thickened, and the lobules just beneath are very atrophic and the periportal tissue shows proliferation, small-celled infiltration and new bile-duct formation, the picture being that of a localized atrophic cirrhosis. These cirrhotic changes are found only beneath the capsule.

Prostate and Seminal Vesicles: Extreme dilatation of all vessels with fibroid hyperplasia. In the seminal vesicles are a number of retention cysts. Spermatic and prostatic plexuses show extreme angiectasia.

Testes: Intense congestion and edema. Diminished spermatogenesis. Increase of stroma. Thickening of basement membrane. Early syphilitic orchitis fibrosa.

Lymph Nodes: All lymph nodes show excessive dilatation of the vessels, many of the retroperitoneal nodes resembling angiomas. Atrophy of lymphoid tissue and increase of stroma.

Semilunar Ganglia: Extreme dilatation of vessels, increase of interstitial tissue and pigmentation of the ganglion cells.

Bone-marrow: Tibiæ contain congested fatty marrow, with small islands of red-cell forming tissue. The sternal and rib marrow shows marked lymphoid hyperplasia.

Adipose Tissue: Reversion to fetal type. Congested and edematous.

Purpuric Spots: Telangiectasias.

Pathological Diagnosis. Plethora vera, "Osler-Vaquez disease" (erythremia; chronic cyanosis and splenic enlargement), secondary to syphilitic atherosclerosis of pulmonary arteries; emphysema and brown induration of lungs; cardiac hypertrophy and dilatation; chronic fibroid myocarditis; syphilitic aortitis; chronic interstitial gastritis; atrophy of pancreas with chronic interstitial pancreatitis; chronic syphilitic orchitis; chronic congestion of all organs; nutmeg liver; chronic splenic congestion; hypertrophy of kidneys with chronic parenchymatous nephritis; chronic leptomeningitis; multiple telangiectasias of skin; hyperplasia of bone-marrow. Latent syphilis; bronchopneumonia; old trichinosis.

Epicrisis. This case presents the complete symptom and pathologic complex of the Osler-Vaquez disease, in the form of a chronic cyanosis, high degree of erythremia and splenic enlargement, with the secondary phenomena of dyspnea, visual disturbance, gastrointestinal symptoms, general weakness, congestion, edema, etc. What is of great importance is the fact that the autopsy revealed a condition to which the Vaquez symptoms are most probably secondary. It can be very reasonably argued that, as the consequence of a widespread lesion of the pulmonary vessels, deficient oxygenation of the blood-stream was produced. As a result of the need for oxygenation secondary emphysema, hypertrophy of the right heart and increased activity of the bone-marrow developed as *compensatory conditions*. The *cyanosis* is an expression of the urgent need for oxygen; the *erythremia* is a compensation for this need; while the *splenic enlargement* is but a secondary result of the plethora and increased blood formation and destruction. The erythremia itself

is brought about by an increased activity (hyperplasia) of the bone-marrow.

Further, the microscopic study of this case shows also the ultimate cause of the whole complex, in that the lesion of the pulmonary vessels presents the characteristics of a syphilitic mesarteritis. This diagnosis at present rests upon the histologic features alone. Levaditi studies of this material have just been made, but no spirochætæ have as yet been found. Additional evidence of the presence of a syphilitic infection is to be found, however, in the characteristic myocarditis, mesaortitis, pancreatitis, adrenal infiltrations, chronic orchitis, and possibly also the chronic leptomeningitis. While the hospital records yield only negative statements as to the occurrence of a syphilitic infection in this patient, a letter from Dr. Frank Smithies, now of the Augustana Hospital, Chicago, tells me that this patient was one of the first to receive a Wassermann test in his laboratory, in Ann Arbor, and that the reaction was positive. From my own standpoint, however, the histologic complex of heart, vessel, pancreas, adrenal and testicular changes can mean but one thing—a latent syphilitic infection. In the meantime, however, the search for the spirochætæ will be carried on.

The degree of arteritis, sclerosis, and atheroma of the pulmonary artery and its branches shown by this case, is, I believe, unique. I have been unable to find in the literature any description of pulmonary sclerosis in which the lesions appeared to be so severe and extensive. In the case reported by me, "Syphilis of the Pulmonary Artery: Syphilitic Aneurysm of the Left Upper Division: Demonstration of Spirochætæ Pallida in Wall of Artery and Aneurysmal Sac," (3) the sclerotic changes in the left upper branch were as marked, but in the other branches the degree of change was much less. The microscopic appearances of the pulmonary vessel lesions were identical with those in this case, and the demonstration of the spirochætæ was accomplished, both in the artery wall and in the aneurysm.

The literature of pulmonary arteriosclerosis is rapidly increasing, particularly in Spanish-American reports. In tropical countries clinical cases of pulmonary arteriosclerosis seem to be more common, and syphilis is regarded as the common etiological factor. In my previous article I collected 4 cases of gumma of the pulmonary

artery, 5 cases of gummatous arteritis, 15 cases of pulmonary arteriosclerosis regarded as syphilitic from the histologic appearances or the association with other evidences of syphilis, and 51 cases of aneurysm of the pulmonary artery in which a syphilitic etiology was probable. (4) In one of the reports (5) it is stated that pulmonary arteriosclerosis is not a rare cause of fatal dropsy in Bengal, and Rogers expresses his belief that when it occurs between the ages of twenty and forty syphilis is the etiological factor.

Sanders (6) reports one case from Dürck's laboratory, and collects seven cases from the literature (Klob, Crudeli, Wolfram, Romberg, Mönckeberg's two cases, and Kitamura) of a primary sclerosis of the pulmonary arteries with associated hypertrophy of the right heart. These were the only reports of such a complex that he was able to find. The cases are incomplete, both as regards clinical history and pathological study, in so far as the question of a syphilitic etiology is concerned. It was apparently excluded or not considered. Romberg's case was characterized clinically by *dyspnea, cyanosis,* and *enlargement of liver and spleen.* No mention of the blood findings. Mönckeberg's Case I likewise showed *cyanosis,* with prominence of eyes, and edema. His second case, a man of fifty-six years, presented marked *cyanosis, edema, dyspnea, palpitation,* with *enlargement of liver.*

Although these cases are incomplete, and the condition of the blood is not stated, it seems probable that some of them, at least, fall into a class showing the syndrome of *chronic cyanosis, dyspnea, erythremia,* and *pulmonary sclerosis* recognized in Spanish-American literature as "Ayerza's Disease" (Cardiacos Negros), from the fact that in a lecture given in his clinic in 1901, Abel Ayerza, Professor of Clinical Medicine, National University of Buenos Aires, was apparently the first to recognize the clinical entity of this syndrome. As far as I have been able to discover the first published use of the term "Ayerza's Disease" is in a Doctoral Thesis, by Dr. C. A. Marty, "La Tensión Arterial en la Tuberculosis Pulmonar," Buenos Aires, 1909, p. 45, in which he says that there is a special group of cases worthy of attention because of increased pulmonary arterial tension associated with hypertrophy of the right heart, pulmonary arteriosclerosis and chronic cyanosis, described eight years previously by Ayerza as "cardiacos negros." The designation is also

used by Escudero in his "Conferencias Clínicas," Buenos Aires; and by Garcia del Real, in "Tratado de Patología Médica," Madrid, 1917, IV, 495–530.

Barlaro (7) reports "A Case of Ayerza's Disease," characterized by *extreme cyanosis, asthma, intense dyspnea, cardiac hypertrophy, erythremia* (red cells 6,600,000), *enlargement of liver, spleen not palpable, Wassermann* + + + + + with *pulmonary arteriosclerosis.* He discusses the differential diagnosis of Vaquez's and Ayerza's diseases, and concludes that many cases of Vaquez's disease are really cases of Ayerza's disease. He so regards the first case reported by Vaquez, the case of Parkes Weber and Watson, Vaquez and Laubrey, Saundby and Russell, Osler (emphysema without splenic enlargement), Herringham, and others. Barlaro's point seems to be that cyanosis and bronchial-pulmonary dyspnea have nothing to do with a primary polycythemia; if they exist in association, the explanation of the condition is to be sought in conditions of the pulmonary artery (Ayerza's disease). While his case was undoubtedly one of syphilis, Barlaro is not sure that all cases of Ayerza's disease are syphilitic or secondary to a parenchymatous lesion. He draws an analogy to Raynaud's disease, and thinks "Raynaud's disease in the lungs" might account for some of the cases presenting the Ayerza syndrome.

The most complete description of the Ayerza syndrome is to be found in the monograph "Esclerosis Secundaria de la Arteria Pulmonar (Cardiacos Negros)," by F. C. Arrillaga, 1913, Buenos Aires. Eleven cases of pulmonary sclerosis with extreme cyanosis, dyspnea, and erythremia (in five cases in which a blood count was made) are described, beginning with the case seen by Ayerza in 1901. The author concludes that there can be no doubt as to the existence of a morbid entity called "cardiacos negros," and first described by Ayerza in 1901, characterized by *cyanosis, hyperglobulism, dyspnea, cough with expectoration of muco- or mucopurulent sputum, headache, angina hypercyanotica, hemoptysis, vertigo, somnolence, etc.* The patients present first a pulmonary evolution extending over a long period, then an evolution of the cardiacos negros state lasting as a rule two to five years. The patients can die sleeping, without edema, after presenting a gallop rhythm of the right heart; or death may take place from early myocardial degeneration with marked anasarca, or from a complication, the most common of

which is broncho-pneumonia. The chief diagnostic points in distinguishing from other forms of cyanosis are the classical history of antecedent symptoms and the *tempo* of evolution of these, and the fact that the cyanosis is acquired, and not the final episode of an asystolic condition as in other forms of cyanosis, but is an initial symptom. The enormous hypertrophy and dilatation of the right heart is the most important objective sign in favor of a pulmonary rather than a peripheral obstruction. Radiography easily settles the diagnosis. The radiographic examination shows a low heart shadow, elongated and broadened, with rounded, elevated apex; the right border of the right ventricle extends far to the right of the sternum. Above the left border of the heart, at the base, is a convexity due to the left auricular appendage, above this the large shadow of the dilated pulmonary artery, and higher the normal shadow of the aorta. Points of differential diagnosis between acute dilatation of the heart and Ayerza's disease are shown by the *tempo* of evolution and the immense dilatation of the peripheral veins in the former condition, while the "cardiacos negros" have "almost no veins." As to the etiology, the lesions in the pulmonary vessels may be secondary to chronic pulmonary disease, bronchitis, tuberculosis, pleural adhesions, or any condition producing a final emphysema; or it may be the result of slow infections, as syphilis, or malaria, or the result of intoxications.

Summary. I am of the opinion that the clinical and pathological study of the case given in this paper separates it from the Vaquez group of erythremias into the class that Ayerza first pointed out as a distinct clinical and morbid syndrome. The long pulmonary evolution of the symptoms in the form of asthma and dyspnea, the later slow evolution of the cyanosis, erythremia, and secondary symptoms are characteristic of the Ayerza cases. The autopsy revealed a unique picture of extreme atherosclerosis of the pulmonary arteries, and the microscopic study shows the picture of a latent syphilis. The radiograms should have revealed the condition at first, had anyone at that time heard of Ayerza's disease and had thereby been enabled to make a correct interpretation of the radiographic findings. The original radiograms have disappeared, but a pencil sketch which remains of the shadows seen and interpreted as a mediastinal tumor is almost a duplicate of the radiographic

illustration, Fig. IX, in Arrillaga's monograph, in which the shadow of the dilated pulmonary artery is very well shown.

The erythremia in Ayerza's disease is beyond question a secondary compensatory process, an increased functional activity of the bone-marrow to meet the deficiency in oxygen supply due to the obstructed pulmonary circulation. It is most probable that this is the case in all forms of Vaquez's disease; certainly in all of those in which there is cyanosis and dyspnea. Neither one of these symptoms belongs to a primary erythremia; and when they are present it is certain that the erythremia is secondary. Likewise, the splenic enlargement is not an essential feature of the syndrome; it is also secondary, and its appearance in the disease may be early or late, according to varying conditions of congestion and increased splenic function. Cases of congenital defects of the septum of the heart have been reported, showing the highest degree of erythremia, cyanosis, and marrow hyperplasia—the essential features of the Osler-Vaquez disease; and the same complex may arise as the result of other conditions leading to a chronic oxygen deficiency.

The Osler-Vaquez complex of cyanosis, erythremia, and splenic enlargement is a syndrome having a varied pathology and etiology, and is not a specific morbid entity. From Vaquez's disease there can be separated a group of cases showing the Vaquez syndrome associated with atherosclerosis of the pulmonary arteries, and possessing distinctive clinical and diagnostic features. To this group of cases the designation "Ayerza's disease," or, preferably, "Ayerza's syndrome," should be applied. The case described in this paper is, therefore, the first one of this type to be recognized in this country, and to be reported in English.

BIBLIOGRAPHY

1. *Arch. Int. Med.*, 1912, X, 597.
2. *J. Am. M. Ass.*, 1908, LI, 897.
3. *Am. J. Syph.*, I, 1917.
4. For literature, see article cited above.
5. Rogers, 1909.
6. *Arch. Int. Med.* 1909, III, 257.
7. *Rev. Assoc. Argent.*, 1917, XXVI, 121

DESCRIPTION OF A MINUTE SARCOMA, NECESSITATING REMOVAL OF THE EYEBALL, WITH HISTOLOGICAL FINDINGS

By John E. Weeks, M.D., New York

THE following case is reported because of several unusual features, among which are: (*a*) The growth is the smallest of which I can find a report in literature, for the presence of which an eyeball has been removed; (*b*) an opportunity to observe the progress of the growth from the beginning of its development; (*c*) the location of the growth; (*d*) the site of the development, and (*e*) the participation of the cells of the pigment layers of the retina in the pigmentation of the growth.

October 15, 1910, Mr. F. W. C., age thirty-one, consulted me regarding the condition of his left eye. The patient first noticed slight blurring of the vision of the left eye, accompanied a few weeks later by flashes of light, two months before consulting me. No pain had been experienced.

Status præsens: Right eye normal.

Left eye, anterior segment of globe normal. Vision with a correcting lens equals 20/100 +, slightly eccentric, images distorted. On examining the fundus, a condition was observed at the macula, roughly represented in Fig. 1, *B*. There was apparently a detachment of the retina over the entire area, without any exudation in the retina itself. The outer zone was pale, but in the center there was a brownish area, indicating the presence of a pigmented slightly raised mass. In size the affected area was slightly smaller than the optic disk in all diameters (approximately 1 millimeter in the lateral and in the vertical diameters). The elevation of the mass was 2/3 millimeter. The field of vision was normal in extent, but there was a very small absolute central scotoma, and a pericentral relative scotoma, as represented in Fig. 2.

A tentative diagnosis of neoplasm was made, and the patient was advised to present himself from time to time. In addition to recording the field of vision, careful drawings were made, particularly in reference to the relation of the blood vessels to the various parts of the growth, for the purpose of determining increase or decrease in the size of the mass.

Since an exudation or growth in the chorioid or retina may be due to a number of causes, examination and tests were made to eliminate tuberculosis, syphilis, accessory sinus disease, etc., and mercury and potassium iodide were administered for a number of months. These investigations did not disclose any tangible condition that could stand in a causative relation.

October 28th the elevation of the mass is 1.5 mm.

November 25th, a small hemorrhage has appeared within the lower boundary of the mass.

February 14, 1911, the growth has enlarged appreciably (see Fig. 1, *D*,) elevation 2 mm. There are a number of small hemorrhages along the lower margin, apparently beneath as well as in the retina. As seen with the ophthalmoscope, the size of the mass as compared with the size of the optic disk was greater in the vertical and about the same in the horizontal diameter equal to 2 mm. by 1.5 mm. Since the presence of a neoplasm could not be doubted, enucleation was advised. On consent of the patient this was done without farther delay.

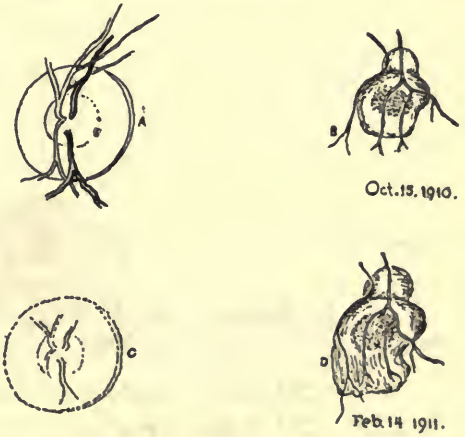

FIG. 1. *A* and *C*, Optic Disk; *B*, Growth when First Observed; *D*, Growth as Observed before Enucleation.

After removing the eyeball it was transilluminated and a slight shadow was demonstrated when the source of illumination passed the posterior pole of the globe. On opening the globe, which was done by a horizontal anteroposterior section in the equatorial meridian, after hardening in formalin, a small brownish mass, apparently of the chorioid, was found at, or very slightly above, the macula. The retina was detached and slightly raised at this point. On measuring, the brownish mass was found to be 1.5 mm. in the horizontal, 1 mm. in the vertical diameters and approximately 0.5 mm. thick, of a very dark brown color (almost black). (See Fig. 3.)

The tissue was hardened in formation, then embedded in celloidin and several sections made of the growth.

The mass was found to be composed for the most part of spindle-shaped cells, some of which are pigmented, and elongated, irregularly shaped

chromophores apparently derived from the retinal pigmented epithelial cells. These cells have multiplied, and some have wandered into or have been carried away from the pigmented layer of the retina by the cells of the tumor in the progress of growth. (See Fig. 4.) The blood vessels in the tumor mass are not numerous, but there are some to be seen mostly

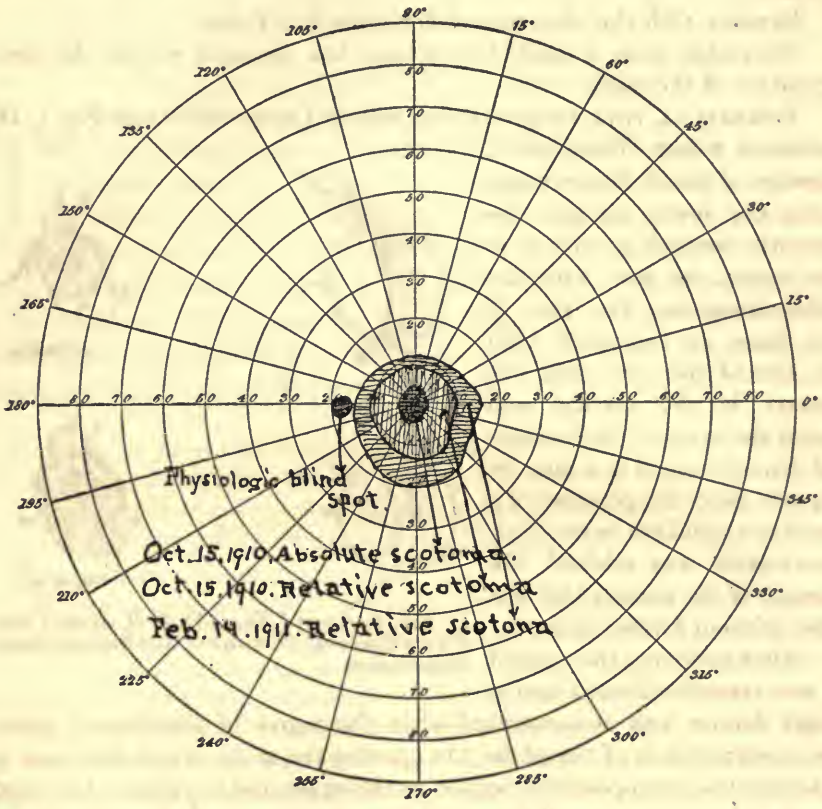

FIG. 2.

situated near the base of the mass. These present the characteristics of blood vessels in sarcoma tissue. A remarkable feature of this tumor is that it is located almost wholly on the inner aspect of the pigment layer of the retina. At one part, at the margin of the tumor mass, there appears to be a break in the continuity of the pigment layer of the retina and the lamina vitrea, and the cells of the choric capillaris and underlying tissue of the chorioid appear to mingle with the cells of the tumor mass. However, I cannot discover any cells that are beyond doubt sarcoma cells in the

tissues of the chorioid posterior to the chorio-capillaris, and the presence of sarcoma cells in the chorio-capillaris is not absolutely certain. This growth, which must be classed with the sarcomata, consists of cells of the connective-tissue type, mingled with chromophores derived from epithelial cells. The connective-tissue type of cells were, in all probability, developed from the chorio-capillaris of the chorioid. The site of the sarcoma is unique so far as I have been able to discover in the literature.

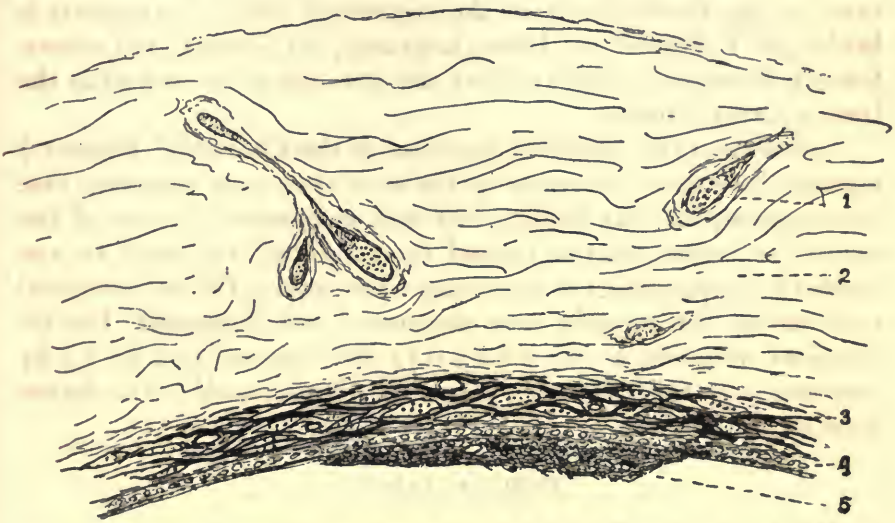

FIG. 3. 1, Section of Short Ciliary Vessels; 2, Sclera; 3, Chorioid; 4, Choriocapillaris; 5, Tumor.

In regard to the origin of sarcoma of the chorioid, Fuchs and many others hold that all sarcomata originate in the deeper layers of the chorioid. However, there is a difference of opinion regarding the place of origin of the so-called leuco-sarcomata of the chorioid (as a matter of fact leuco-sarcoma of the chorioid invariably presents some pigment in some part of the growth. Half of the same neoplasm may be deeply pigmented and half almost entirely free from pigment). In the opinion of H. Knapp, (1) Briere, (2) and Schieck (3) these tumors spring from the chorio-capillaris. Leber (4) has raised the question as to whether the pigment epithelium of the retina does not enter into the formation of the pigment in melanosarcomata of the chorioid, and concludes as follows:

1. "A portion of the pigmented cells of melanosarcoma of the chorioid is derived from the pigment cells of the retina . . .

2. "The pigment of these cells is derived from the pigment of the blood, and its presence in the cell is due to a phagocytic action of the cells on the red blood corpuscles. The pigment of the branching pigmented cells of the chorioid is not of hæmatogenous origin."

The opinion that the retinal pigment cells take part in many cases in the development of the pigmented cells in sarcomata is held by E. V. Hüpfel, (5) Leber, Lagrange, (6) Schieck, and others. Schieck, however, is positive that this does not occur so long as the lamina vitrea is intact.

Under the title "Smallest Sarcoma of the Chorioid," Fuchs (7) reports three cases occurring in the eyes that were removed. One post-mortem, the man having died with symptoms of tumor of the brain; the second an eye excised for glaucoma, the third an eye excised for suppuration of the cornea after injury. On microscopical examination the growths were discovered and diagnosed. The dimensions were first 0.7 by 0.8 by 0.15 mm.; second 1.25 by 1.5 by .009 mm.; third 2.25 by 1. by 0.25 mm. All originated in the deeper layer of the chorioid.

BIBLIOGRAPHY

1. "On Intra-ocular Tumors," Wood, N. Y., 1868, 225.
2. "Étud. clin. et anat. sur le Sarcome de la chorioide," Thèse de Paris, 1873.
3. *Graefe's Arch.*, XLV, No. 2, and XLVIII, No. 2.
4. *Graefe's Arch. of Opbth.*, XLIV, 683.
5. *Arch. f. Opbth.*, XL, Nos. 1 and 4.
6. *"Nemeurs de L. Œil,"* Paris, 1901.
7. *Tr. Am. Opbth. Soc.*, XII, 787, 1911.

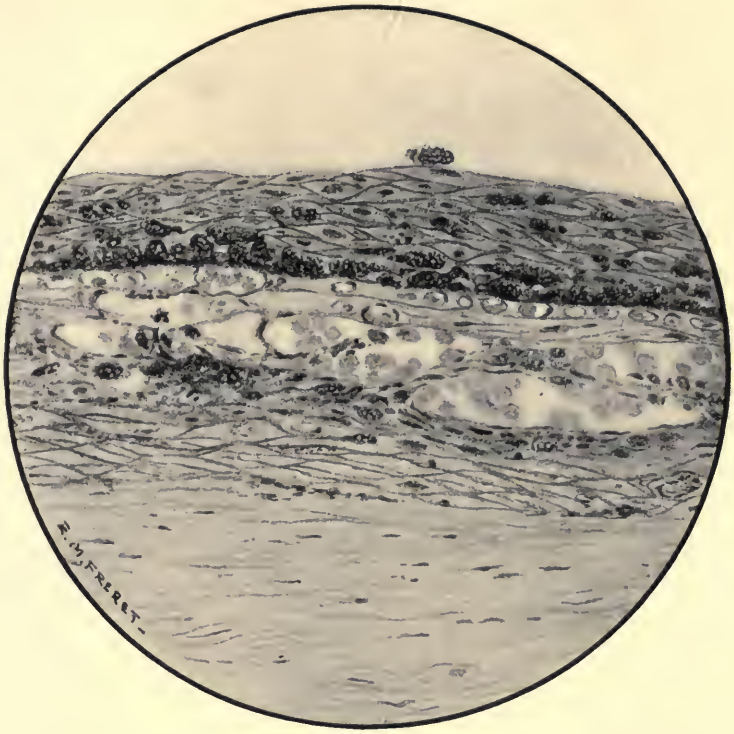

FIG. 4. SECTION OF TUMOR, CHOROID AND UNDERLYING SCLERA.

INTOXICATION OF INTESTINAL OBSTRUCTION

TOXIC PROTEOSES NOT DESTROYED IN INTESTINAL TRACT AND NOT FORMED IN COLON LOOPS

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MUCH has been written about the interesting type of intoxication which develops with an intestinal obstruction. The fact that many explanations have been championed by different investigators and clinical observers is sufficient proof that convincing evidence is not at hand to explain all the observed reactions. We wish to point out several observations and add other experiments which bear on this subject. We believe that some of these facts have been overlooked by some of the recent investigators and that a proper grasp of these data will clear the field of many confusing and apparently contradictory theories.

It is now admitted by practically all investigators in this field that a poison is formed in the body and is responsible for the intoxication which develops. Where this poison develops, what its nature may be, and how it is formed are questions open to debate and have been discussed with much earnestness and even polemical vigor by the many workers who are seeking the solution of this problem. That this intoxication is purely "non-specific" gives it an added interest to many workers, and makes it probable that information gained concerning this intoxication may have value in the proper understanding of the "non-specific" fraction of intoxications associated with bacterial infection.

One most important point has been lost sight of and needs constant emphasis—*Nothing produced within the lumen of the intestinal tract can be directly concerned in the intoxication of intestinal obstruction,* because the intestinal epithelium is impervious to all toxic substances which can be demonstrated in any amount in the material accumulating in the obstructed intestine. Material

obtained from the obstructed intestine can be fed in unlimited quantities or injected into the normal duodenum or obstructed intestine, or into closed loops of the intestine without causing the slightest degree of intoxication. These facts have been demonstrated beyond any doubt in published experiments (1, 2) and the data given below add confirmatory evidence. Therefore we need not concern ourselves with hypothetical toxins which may be produced in the lumen of the obstructed intestine by bacterial growth or by ferment cleavage of protein substances. There is no evidence that any such toxins are formed under the condition of intestinal obstruction, but if they are formed they cannot be concerned in the general intoxication, because these substances cannot be taken up by the intact intestinal mucosa.

We believe that the epithelium of the mucous membrane of the small intestine under obstruction conditions is able to form a toxic substance or substances, and that this poison can be formed only by the intestinal epithelium. Unusual development of intestinal bacteria may act as a stimulant, but the essential thing is that the toxic substance must be *formed in the mucous membrane.* As the poison is being formed in the mucosa of the small intestine a part of it is taken up by the blood stream and causes the characteristic clinical reaction, a part is not taken up, but is excreted into the lumen of the gut, and once in the intestinal lumen the poison is *inert* in so far as the host is concerned. This portion of the poison may be obtained from the material in the lumen of the obstructed intestine. It is to be kept in mind that this poison is not found in the normal intestine.

The substance or substances which we have isolated from obstruction material have been described in other communications (3) (4). It is sufficient to say that the evidence points to the proteose group of substances, and we shall use the term "proteose" with proper mental reservation to indicate the possibility of other large molecular substances being present in the "proteose mixture."

EXPERIMENTAL OBSERVATIONS

Closed Loop of Colon. Duration Ten Months. Dog 18–8. Collie. Healthy Female. Weight 25 pounds. July 19, 1917. *A closed loop of colon* done in the usual way by Dr. Woolsey and Dr. Kerr. The loop included about

3 inches of the ileum and all of the colon up to about 5 inches from the anus. The ends were cut across and inverted. A lateral anastomosis was made between the ileum and rectum to re-establish the intestinal tract.

July 23d to 31st. Uninterrupted convalescence. Weight 25 pounds.

Oct. 3d. Dog is normal and lively. Weight 29.5 pounds. Isolated in metabolism cage without food.

Oct. 4th. A small amount of fecal material removed from cage and discarded.

3 P.M. *A solution of toxic proteose, 200 c.c., given by stomach tube.* Obtained from autopsy 17–60, described below.

Oct. 5th. 10 A.M. Dog normal in every respect. No feces.

Again *given 200 c.c. of a solution of toxic proteose.* Autopsy 17–60. There is no clinical reaction following either administration of proteose.

2 P.M. Soft yellow semi-fluid feces passed and immediately collected from cage. Weight 50 grams.

Fecal material dissolved in water (about 100 c.c.), separated by centrifuge and the supernatant fluid precipitated by five volumes of 95 per cent alcohol. This alcoholic precipitate dissolved in distilled water, slightly acidified and boiled, then filtered to remove a small amount of precipitate. This neutralized watery extract of the alcoholic precipitate was shown to contain much toxic proteose-like material tested on Dog 18–57. This dog was severely but not fatally intoxicated. See below.

Oct. 6th, 10 A.M. Soft semi-fluid yellow *feces, 30–40 grams* in weight, collected carefully and extracted for proteose exactly as described for preceding day. This material tested on Dog 18–58 gave a lethal and typical intoxication, fatal within five hours. The autopsy findings were typical of acute intoxication following the intravenous injection of proteose material obtained from cases of intestinal obstruction.

12 M. Dog given 200 c.c. milk by stomach tube. Dog normal in all respects.

Oct. 7th. No feces passed.

Oct. 8th. 10 A.M. Soft semi-fluid yellow *feces, 50 grams* in weight, collected as usual and extracted for proteose-like material exactly as described above. This extract was tested upon Dog 18–55 and was shown to contain no toxic material whatsoever. (*Control period.*)

Mar. 11, 1918. Dog 18–8 in normal condition. Weight 30.8 pounds.

May 15th. Dog is not in good condition and shows evidence of definite intoxication. Abdomen is prominent. Weight 32 pounds.

May 17th. Dog is very sick. Abdomen distended. Vomiting. Ether anesthesia and sacrifice.

Autopsy performed at once. Thorax, heart, and lungs normal. Peritoneal cavity contains 3000 c.c. turbid straw-colored fluid with a sediment of granular material, the granules of fibrin measuring 2 to 3 mm. in diameter. Serous surfaces are injected and swollen, the omentum particularly. Stomach contracted and normal; small intestines collapsed and normal throughout; the anastomosis between the ileum and colon is imbedded in a mass of dense adhesions which contain some pus pockets. This long latent period is of some surgical interest. These foci of infection undoubtedly explain the general peritonitis. Spleen is somewhat enlarged and mottled. Liver pale and yellow and contains two superficial small pus pockets just beneath the capsule anteriorly. This is the result of an extension of the inflammatory process from the peritoneum into the parenchyma. Pancreas and kidneys are normal.

Loop of Colon. Its walls are definitely hypertrophied, particularly in the short stump of the ileum. There are very few adhesions over the serous surfaces. The mesentery is thick and tendinous. Mucous membrane is normal, perhaps a little thickened. The inverted ends are clean and the most careful examination shows no ulcers anywhere. The ileum measures 3 inches in length and contains only traces of yellowish fecal-like material. A large sausage-like mass of material was packed into the lower colon. This material is putty-like in consistency and of a dark slaty color. It separates very easily and cleanly from the mucous membrane. It is homogeneous throughout.

Microscopical sections in general are negative. Liver shows a little central fatty degeneration. Sections from the stomach, intestines and various parts of the closed loop show normal epithelium everywhere.

Material from closed loop weighs 126 grams. It was ground up in about 250 c.c. of distilled water, sand being added in the mortar. It was reduced to a thin soupy fluid and then shaken for hours in the shaking-machine. All particles were thrown down by the centrifuge, giving a supernatant fluid of opalescent gray appearance. This was precipitated with five volumes of 95 per cent alcohol. After standing for two days the alcoholic precipitate was dissolved in water (700 c.c.), made slightly acid to litmus with acetic acid, brought to a boil and filtered. The filtrate was concentrated over a water-bath after neutralization to 100 c.c. All of this material was given intravenously to Dog 19–19. There were no evidences of intoxication. See below.

Toxic Proteose from Case of Human Obstruction, Autopsy 17–60. Young adult male; operation upon lower ileum. Shortly after this operation evidences of intestinal obstruction developed with very rapid intoxication and death. Autopsy was performed within two to three hours

post-mortem. A kink in the ileum was found just above the enterostomy wound.

Intestinal fluid was obtained in large amounts from the distended ileum. This material had the usual appearance and odor characteristic of such material. It was cleared by the centrifuge and the watery broth-like fluid material was poured into five volumes of 95 per cent alcohol. After several days the alcoholic precipitate was taken up in distilled water, acidified with acetic acid, brought to a boil, and filtered. This clear amber filtrate was neutralized and tested out on a normal dog, 18–43. Weight 27 pounds. Ten c.c. per pound body weight given intravenously gave a very severe, almost fatal, intoxication with repeated vomiting, bloody diarrhea, and prostration. This material (4000 c.c. in all) was then concentrated to 2000 c.c., autoclaved, and preserved. It is obvious that 5 c.c. per pound body weight should approximate a lethal dose. This human material, containing much of the characteristic poison, was given by stomach tube in considerable doses to the dog 18–8, used in the first experiment.

Proteose Recovered from Feces after Administration by Mouth. Dog 18–57. Fox-terrier, adult female. Weight 24.3 pounds.

Oct. 29th, 12 M. Ether anesthesia and intravenous injection of *proteose extract obtained from Dog 18–8; fecal material of Oct. 5th.* 200 c.c. total amount of deep amber-colored fluid. This injection caused little depressant effect on blood pressure.

12:40 P.M.—Temperature 38.3. Passed solid feces.
2:00 —Temperature 38.0.
2:30 —Temperature 38.4. Diarrhea and vomitus.
3:20 —Temperature 38.8. Dog very sick. Bile-stained vomitus.
3:50 —Temperature 39.1. Continuous vomiting and diarrhea.
4:45 —Temperature 39.2. Vomiting continuous.
5:30 —Temperature 39.1. Clinical improvement.

Oct. 30th: Dog appears well.

This experiment shows that toxic proteose material from a case of intestinal obstruction, fed to a dog with excluded large intestine, may be recovered unchanged from the feces. There is no resultant intoxication from feeding this poison. The toxic proteose is able to resist the action of the digestive enzymes of the stomach and small intestine for a period of forty-eight hours or longer. We have reported (5) experiments to show that this toxic substance is able to resist long periods of digestion *in vitro.*

Proteose Isolated from Feces after Administration by Mouth. Dog 18–58. Fox-terrier, small adult male. Weight 12.8 pounds.

Oct. 29th, 12 M. Ether anesthesia and intravenous injection of *proteose extract obtained from Dog 18–8. Fecal material of Oct. 6th.* 150 c.c. total amount of amber-colored opalescent fluid.

12:40 P.M.—Temperature 38.0. Mucous diarrhea.
2:00 —Temperature 38.0. Mucous diarrhea and bile-stained vomitus.
2:30 —Temperature 37.7. Vomitus and diarrhea, prostration.
3:15 —Temperature 37.6. Prostration. Pulse very weak.
3:50 —Temperature 36.8. Condition unchanged.
4:50 —Temperature 36.4. Profound intoxication.
5:20 —Death and autopsy immediately.

Blood obtained in oxalate solution showed practically no plasma on standing. This blood concentration is very common in severe proteose intoxication. Thorax, heart, and lungs normal. Liver, spleen, pancreas, and kidneys are swollen and engorged with blood. Stomach shows a pale pyloric mucosa and pink swollen cardiac mucosa. Mucous secretion is very abundant. Duodenum, jejunum, and ileum present a deep purple velvety mucosa coated with a thick layer of mucus. Colon shows definite engorgement. This *autopsy is in every way typical* of acute intoxication resulting from a lethal dose of the proteose obtained from an obstructed intestine.

This experiment confirms in every respect the preceding observation. There seems to have been little destruction or loss of the toxic proteose and its toxicological reaction is identical with that of the original material before passage through the intestinal tract. Such resistance toward the digestive enzymes is remarkable.

Proteose Absent from Feces. Control Experiment. Dog 18–55. Spaniel, small adult female. Weight 19.3 pounds.

Oct. 22, 11 A.M. Ether anesthesia and intravenous injection of *proteose extract obtained from Dog 18–8. Fecal material of Oct. 8th.* 120 c.c. total amount obtained as described above. This injection caused a transient fall in blood pressure, but no change in the temperature curve. There were no clinical signs of intoxication at any time.

These control feces contained no toxic material in any way comparable to the material isolated and tested in the two preceding experiments. These feces were collected from the same dog, 18–8, with the exception that milk was given by stomach tube instead of the proteose solution. This experiment gives the necessary control

to the two preceding observations and substantiates other observations to show that the normal intestinal tract contains no toxic proteose material.

Proteose Isolated from Colon Loop Material Non-toxic. Dog 19–19. Mongrel, adult male. Weight 23.3 pounds.

Aug. 13th, 12 M. Ether anesthesia and intravenous injection of *proteose extract obtained from the colon loop* material of Dog 18–8. The entire proteose extract made as described above, concentrated to 100 c.c., given slowly intravenously. This injection caused only a slight fall in blood pressure with considerable flushing of the skin. It caused no temperature reaction of any appreciable degree and not the slightest evidence of clinical intoxication.

Compare with the several experiments given just below to show that these colon loops are non-toxic and do not form toxic proteose-like substances.

Closed Loop of Colon. Duration Four Months. No Intoxication. Dog 17–111. Airedale, young adult female. Weight 22 pounds.

Jan. 3d. Dr. Woolsey isolated *a closed loop of the colon* as described above and established the intestinal tract by anastomosis between the ileum and the rectum.

Jan. 5th to 8th. Normal recovery. Weight 19.3 pounds.

Feb. 2d. Dog normal and regaining lost weight. Weight 21.8 pounds.

May 1st. Dog has been uniformly in good condition. Weight 27.8 pounds. There has been no evidence of any intoxication at any time. Dr. Woolsey and Dr. Kerr *excised the loop of colon* with no operative difficulty.

Loop of Colon includes 1 inch of ileum which is empty. The cecum is empty. The lower end of the colon loop contains a large sausage-like mass which has the general appearance and consistency of normal feces. It is uniform and pasty throughout and separates cleanly from a normal pale mucous membrane. The lower end of the colon where inverted shows one tiny ulcer, not over 2 mm. in diameter. Without exception the mucosa elsewhere is pale, normal, and intact. The microscope shows a normal mucous membrane except for the tiny superficial ulcer described above. Goblet cells and mucus are conspicuous.

Colon Loop Material (about 150 grams in weight). It was ground with water and sand to a thin soupy mixture, the final volume about 400 c.c. This was not centrifuged, but poured direct into five volumes of 95 per cent alcohol. The alcoholic precipitate dissolved in water (about 1200 c.c.)

slightly acidified with acetic and brought to a boil. The precipitate was removed by means of the centrifuge, giving a grayish opalescent fluid somewhat like clam broth. This material was neutralized and tested out upon a number of normal puppies.

Material from Closed Loop of Colon. Dog 17–111. Tested by intravenous injection upon the following animals:

Pup 17–207. Weight 14 pounds. 2 c.c. per lb. intravenously. No intoxication.

Pup 17–181. Weight 14.3 pounds. 7 c.c. per lb. intravenously. No intoxication.

Pup 17–217. Weight 10.3 pounds. 8 c.c. per lb. intravenously. Slight intoxication.

This last experiment (Pup 17–217) showed a little clinical intoxication and slight febrile reaction. The amount injected was very large for a small puppy, but it may indicate a trace of toxic material in this closed loop.

Proteose Absent in Feces after Colon Extirpation. Dog 18–42. Fox-terrier, adult female. Weight 12.8 pounds.

Sept. 27th, 12:30 P.M. Ether anesthesia and intravenous injection of *proteose extract obtained from feces of Dog 17–111.* Thin yellow feces (123 grams in weight) obtained fresh from cage, ground up and extracted with 400 c.c. distilled water, agitated in shaking-machine for five hours and separated by centrifuge. The opalescent yellowish broth-like fluid poured into five volumes of 95 per cent alcohol. After two days the alcoholic precipitate extracted as usual with water, acidified, brought to a boil, filtered, and concentrated over the water-bath to 150 c.c. The final solution was almost clear, pale amber in color. Total amount of this extract was given intravenously with definite but moderate depression of the blood pressure. There was a slight febrile reaction, but no definite clinical shock and no signs of the usual intoxication.

This experiment gives confirmatory data to show that toxic proteoses are not present in the small intestine of the dog. The colon extirpation makes the collection of soft feces very easy and excludes the possibility of any neutralizing action taking place in the colon.

Discussion. The experiments outlined above are capable of but a single interpretation. It is quite clear from these experiments and other similar observations which need not be recorded at this time, that closed colon loops are never associated with any definite clin-

ical intoxication referable to the closed loop. This is very different from closed loops of the small intestine which invariably are associated with distinct evidences of intoxication. Closed loops of the colon cause no disturbance even if isolated for many months (four to ten or longer). Material accumulates slowly in these loops, and this material looks remarkably like normal fecal material. It is made up mainly of cell debris and masses of bacteria. No toxic proteose material can be isolated from this colon loop material. Again, this differs from the material which accumulates in a closed loop of small intestine as such material is rich in toxic proteose. It is obvious, therefore, that the colon cannot take any active part in the intoxication of intestinal obstruction.

The proteose material isolated from an obstructed intestine or closed intestinal loop is known to be resistant to digestion *in vitro* (*5*). These experiments show conclusively that this same proteose material can resist the digestive enzymes of the intestinal tract of the dog for forty-eight hours or longer. It is possible to recover this proteose from the feces after its administration by stomach tube.

These experiments give more evidence to prove that these toxic proteoses are not present in the small intestine of the normal dog. A study of the fecal material obtained from dogs whose colons have been removed shows that a toxic proteose is not present in the small intestine and excludes any neutralizing action on the part of the colon.

BIBLIOGRAPHY

1. Whipple, Stone, and Bernheim, *J. Exper. M.*, 1914, XIX, 166.
2. Davis, D. M., *Johns Hopkins Hosp. Bull.*, 1914, XXV, 33.
3. Whipple, Rodenbaugh, and Kilgore, *J. Exper. M.*, 1916, XXIII, 123.
4. Whipple and Van Slyke, *J. Exper. M.*, 1918, XXVIII, 213.
5. Whipple, Stone, and Bernheim, *J. Exper. M.*, 1913, XVII, 307.

SOME EXPERIENCES AND OBSERVATIONS IN THE TREATMENT OF ARTERIOVENOUS ANEURYSMS

BY THE INTRASACCULAR METHOD OF SUTURE (ENDOANEURYSMORAPHY), WITH SPECIAL REFERENCE TO THE TRANSVENOUS ROUTE. (A SUMMARY)

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WITHOUT attempting a general discussion on the treatment of arteriovenous aneurysms, which would be beyond the scope of this contribution, it is my purpose to give a brief account of a group of personal experiences which illustrate the practical application of the intrasaccular methods of suture which I have so long advocated for the cure of arterial aneurysms (endoaneurysmoraphy), and which I have found equally, if not more, advantageous, in the cure of arteriovenous aneurysms.

Of course there is no single method or technic that is applicable to all varieties of arteriovenous aneurysms as these are met in practice. There are, and always will be, cases in which the conservative principle of the suture, which aims at the restoration of the functional integrity of the blood vessels, will have to yield, in the presence of insurmountable and forbidding anatomical and pathological conditions, to the radical methods of ligation and extirpation, which are also to be regarded as conservative whenever they accomplish their purpose (cure) without sacrifice of limb or life. But the experience of the author confirms the opinion that by the adoption of new technical suggestions, such as exhibited in this paper, the opportunities for the application of a conservative technic can be much enlarged, thereby reducing very considerably the number of radical ligations and extirpations which are undoubtedly performed with unnecessary frequency and severity in the current practice of the day.

It would be well to premise a further consideration of this

subject by stating that in dealing with the latest suggestions presented in these personal experiences, we have in mind the treatment of the fully formed or established types of the mature arteriovenous lesions as distinguished from the primary or recent wounds of these vessels, when the question of primary hemostasis for hemorrhage or the relief of rapidly spreading hematomas are the first consideration. Even in these, the principle of conserving the functional integrity of the injured vessels is seriously to be considered, and can be successfully met, in many instances, by the devices of conservative practice—such as end-to-end suture of the vessels, vascular grafts, and intubation with paraffined glass or metallic tubes (Brewer's, Tuffier's, Lespinasse's, et als.). But the technical problems are very different from those offered by the mature or established arteriovenous aneurysms.

If we were to study clearly the morphology and pathological anatomy of the more mature and fully established arteriovenous aneurysms, we would probably be able to differentiate more than twenty varieties. These, however, can be grouped about the two fundamental types, which have been classical since the days of Wm. Hunter and Scarpa. These are the *aneurysmal varix* (Varix aneurysmaticus) and the *varicose aneurysm* (aneurysma varicosum). The aneurysmal varix, with its subvarieties, typifies the *direct* mode of arteriovenous anastomosis; the varicose aneurysm, the *indirect* communication between the two vessels, through a common or intermediary sac. In the aneurysmal varix the arterial and venous wounds become agglutinated and adherent as a direct inosculation, following as an immediate or early sequel of the injury, and an arteriovenous fistula is established after the small perivascular extravasation has been absorbed. Two important subvarieties of this type must be distinguished: (1) The true aneurysmal varix which presupposes a varicose dilatation of the vein, constituting the sac of the aneurysm, and which, owing to the progressive dilatation of the vein, may attain enormous proportions, not only at the seat of the anastomosis, but far beyond the proximal and distal sides of the abnormal communication; and (2) the simple arteriovenous fistula (*phlebartery* of Broca), in which there is no varicose dilatation except a general symmetrical enlargement or ampullar formation of the vein at the site of the fistula.

In the *varicose* aneurysm, as classically described, the normal anatomical position of the vessels is disturbed; they do not lie side by side as in the aneurysmal varices. The injury is followed by more or less extensive hemorrhage which, being circumscribed by the resistance of the perivascular tissues, forms a well-defined pulsating hematoma and finally an encysted and clearly differentiated and well-walled sac, which is lined with endothelium continuous with that of the open mouths of the blood vessels.

As above stated, it is customary to describe a varicose aneurysm as an intermediary sac formed and interposed between the injured vessels, through which an indirect communication is established between the artery and vein. But contrary to this teaching, all surgeons of experience will agree that the formation of this *intermediary* sac is an exceptional occurrence, whereas the presence of a well-defined sac into which the injured vessels open *separately* without any disturbance in their anatomical relations—the two vessels lying side by side—is a common occurrence. On opening such a sac and evacuating the clot, the two vessels will be seen at the bottom or at some part of the periphery of the cavity, plainly in relief, or faintly outlined under the fibro-endothelial capsule, which, in old aneurysms, covers them like a veil. The orifices indicating the original seat of injury will show themselves in various ways—either as elliptical or slit-like openings lying parallel to each other, or as quadruple groups, two proximal and two distal, separated by an interval of variable length. The proximal orifices represent the cardiac, and the distal, the peripheral ends of the divided vessels. These different appearances depend upon the extent of the primary injury—whether a partial or a total division of the vessels is involved in the trauma. In some rare cases, in which the vessels have been completely divided, there are, as Amussat first observed, only two recognizable openings leading into the sac, one for the artery and one for the vein, which indicate the cardiac or central ends of the divided blood vessels, the peripheral ends having been occluded by thrombi and finally lost in the wall of the sac. It is more frequent, in our experience, to see a type of varicose aneurysm, following partial division of the vessels, in which there is a common, fairly large sac, which, when opened, exhibits a smaller pocket formed by the sheath of the vessels. In the center of this smaller cavity four

orifices appear in close proximity, showing that the vessels have been injured tangentially and simultaneously, either by stab or shot—causing no disturbance in their relations, as they lie side by side in perfect apposition. The four orifices lie parallel to each other, two above and two below, and open directly into the smaller sac formed by the sheath which has been torn open, leaving a circular or elliptical opening which merges in its contour with the larger pseudo sac formed by the primary hematoma.

The margins or orifices in all types of arteriovenous aneurysms of mature formation (six or eight weeks, and over) are usually thick and smooth, and are covered by a glistening endothelium which merges and is continuous with the endothelial lining of the cyst-like cavity of the sac. The same blending or merging with the endothelial lining is observed in the fistulous communications existing in the direct arteriovenous lesions, a matter of importance, as this thickened and firm lining offers an excellent grip for the sutures which obliterate the anastomotic communications.

Another and most troublesome, but rarer, type is the arteriovenous aneurysm in which the artery has been injured simultaneously with its two satellite veins. In these cases a venous sac or ampulla is formed on each side of the artery. The two venous sacs are usually asymmetrical, according to the different planes of resistance encountered in their development, one of these attaining large proportions, and the dimensions of the other being only moderate.

In other, still rarer, cases, more often met in civil practice (hunting accidents), and fortunately limited, usually, to the peripheral vessels of a secondary order (upper extremity), are those in which an artery is injured simultaneously and at many places by fine shot. In these cases the condition imitates cirsoid aneurysm, and the arteries and veins are mixed up in such inextricable confusion that extirpation is the only remedy; fortunately they seldom attain dangerous proportions or cause serious disabilities, and can be safely allowed to remain undisturbed.

Arteriovenous aneurysm with an *arterial* sac, in which the aneurysm ruptures into a vein, is so great a rarity in surgical practice that it can well be relegated to the domain of pure pathology. It is practically observed only in the thorax as a result of pathological

conditions beginning on the arterial side (aortic aneurysm opening into the vena cava, etc.).

Personal Experience with the Suture in Arteriovenous Aneurysms. In a personal experience of over 204 surgical interventions upon the large blood vessels, I find the record of 24 cases of arteriovenous injuries of various types. In this group I have utilized the principle of endoaneurysmoraphy in 12; viz., common carotid (1); external iliac (1); the common and superficial femoral (8); the peroneal vessels (1); the subclavian (1). All of these have made good recoveries, except the carotid aneurysm, in which death occurred on the eighth day after the operation, from coronary disease and pulmonary clot; and in the iliac aneurysm, in which death occurred from mesenteric thrombosis and gangrene of the bowel caused by prolonged compression of a loop of bowel by a powerful Doyen retractor, which had been used in an extensive subperitoneal dissection to expose the iliac vessels. In neither case, as shown by autopsy, was the technic of the operation, as far as the vessels were concerned, responsible for the fatal termination, as the condition of the wound was found to be faultless. In the subclavian case, which was performed September 3, 1900, on a young white farmer, age twenty-four years, the artery, which had been perforated with a bullet in the second division, immediately behind the anterior scalene, had to be ligated on each side of the muscle; but the vein, which was surprisingly small, was sutured. The patient recovered, but lost part of his hand from arterial ischemia and necrosis.

Lateral Angiorapby in Arteriovenous Hematoma. In another case, a white man, age twenty-six years, operated at the Touro Infirmary on May 3, 1907, suffered a gunshot wound involving the femoral vessels in Hunter's canal, and was operated upon about six weeks after the injury, by separate lateral suture of each one of the orifices, leaving the lumen of each vessel pervious. The patient made an excellent recovery, with perfect functional result to the limb, notwithstanding his deplorable condition from many wounds, including multiple fractures of the lower jaw, which he had received in quelling a negro riot at Liberty, Miss. This procedure represents probably the oldest and, undoubtedly, the best-known of the conservative operations that have been applied for the cure of arteriovenous aneurysms, and is an ideal method when it can be carried out. The experience of the recent war will, no doubt, add quite a large number of such cases to the early list of the pioneers (Z. von Manteuffel (1895), femoral vessels; Cammagio (1898), femoral vessels; Gérard Marchant (1898), brachial suture; Peugniez (1900), Matas (1900), subclavian suture), and other civilian and military surgeons who have availed themselves of the progress in vascular surgery at the present day.

The Obliterative Suture in Arteriovenous Aneurysm. Another case, operated on March 8, 1912, was that of a youth of eighteen years from Wesson, Miss., who had been accidentally stabbed, when twelve years old, with a long pocket knife, in the upper femoral region. He had developed an arteriovenous aneurysm which involved the common femoral vessels at the apex of Scarpa's triangle, close to the origin of the profunda. In view of the long duration and possible necessity of doing an obliterative operation, the boy was kept under careful observation for two weeks before the operation. During this time he was well nourished and given digitalis systematically, in the hope of increasing his blood pressure, which was scarcely ever over 110 S. Frequent tests were made of his collateral circulation, which showed that the living color returned to the limb after Esmarch ischemia, while the common femoral was compressed. The living color returned in about five minutes, but just before the operation the time had shortened to three minutes. Feeling that a good collateral circulation had been established, I undertook the operation, believing that, if it became necessary, an obliteration could be performed without risk to the limb. The operation was performed under ether at the Touro Infirmary on March 8, 1912. The incision, directly into the sac, revealed a large, well-lined cavity which was at first taken to be the dilated femoral vein, but which was subsequently interpreted as a pseudo sac well lined with endothelium, which opened directly into a lesser pocket of oval shape, measuring about 2 inches in diameter. At the bottom of this could be seen four separate orifices, each large enough to admit the tip of the little finger and grouped into a quadrilateral, the two openings on the inner side corresponding to the distal and proximal orifices of the femoral vein and the two outer to those of the artery. A ridge or linear induration indicated the original septum of the sheath which separated the arterial from the venous compartment, but the edges of the orifices were continuous and blended with the septum and with the smooth, glistening endothelial surface that lined the interior of the sac. Each one of these orifices was now sutured separately with fine paraffined linen, leaving it completely sealed and obliterated. Then all communications leading from the large vessels to the sac were closed. The sac, which was very densely incrusted all over its walls with calcareous deposits in plaques, was cleared of these incrustations only by prolonged scrubbing with saline solution and gauze sponges. In the main cavity, which formed the bulk of the aneurysm (size of a small apple), a mass of phleboliths was found in the midst of the red clot. After the toilet of the sac had been completed, this was obliterated partially by plication and by infolding of the sac walls with continued rows of fine chromic gut sutures. The blood pressure before the operation (9.40 A.M.) was 110 S.; during the operation it

rose to 120 S and at the close of the operation (10.25 A.M.) it fell again to 110 S. At the close of the operation the Esmarch constrictor, which had been applied high up in the groin, was removed and was followed, in less than one minute, by a return of a good living color throughout the extremity to the tip of the toes. At 10.35 A.M. the dorsalis pedis and posterior tibial could be felt beating distinctly in the foot. Evidently, the preliminary tests of the collateral circulation had told the truth, and the results confirmed our confidence in their value, and justified the obliterative operation which we had adopted.

The records show that the wound healed *per primam.* It was inspected on the fourth day. An ulcer which had existed in the leg as a consequence of the varicosities healed rapidly, and the boy was discharged and returned to his home on March 29th, nineteen days after the operation, with his ulcer healed, a notable reduction in the varicosities, and perfect functional use of the limb.

Since the day of his discharge I have seen the boy repeatedly, and in my last examination, one year ago, there was no trace of the aneurysm, and only a linear scar indicated the site of the operation. The varicosities along the saphenous tract had subsided, the ulcer had remained healed, and even the pigmentation which had darkened his leg had paled. He was working on a farm and doing hard labor as a field hand.

This case illustrates not only the simplicity and safety of the technic of the intrasaccular suture in its *obliterative* phases, but its successful application to a type of varicose aneurysms, which is not infrequent and could be made quite formidable if attacked by followers of the methods of either one of the extreme and divergent schools of vascular surgery,—the ultra conservatives, represented, on the one hand, by the German followers of Lexer (the large majority of the German military operators in the late war), who believe it is their duty to do the so-called "ideale" operation in every case in which it is feasible, and who, taking this case as an example, would have systematically extirpated the sac, dissected out the vessels from their bed and attempted to do an end-to-end suture of both vessels; and, on the other hand, the ultra radicals, represented by the French school of surgeons who, following the lead of Delbet, extirpate the sac, together with its vascular contents, and then ligate the four stumps by the quadruple ligature.

Between these stand the intrasaccular ligaturists of the British and Japanese schools, who do far less damage to the perivascular

tissues, but who, none the less, give themselves unnecessary worry and complicate their technic by dissecting out the vessels in order to close them by the quadruple ligature.

It is possible that by any one of these methods this aneurysm would have been cured and the limb saved, because, in this case, it had been clearly demonstrated that the collateral circulation had been established and that restorative procedures were unnecessary. But why undertake the laborious and, at best, uncertain procedure of a vascular angioraphy, as in the so-called "ideale" operation, or subject the patient to the unnecessary trauma of an extirpation with its waste of good vascular material; or, again, the extrasaccular dissection required by quadruple ligature—when the simple obliteration of the orifices can be so easily accomplished, with so much economy to the blood vessels (including the collaterals)—and the objective attained so easily and safely, by the elementary technic of the suture?

I could easily add to the testimony of the preceding case by a number of clinical experiences which prove the simplicity and reliability of the endoaneurysmal suture in the many phases of *varicose* aneurysm in which the obliterative principle is indicated. Apart from my own experiences, I could quote a number of confirmatory published reports from the practice of my associates and other local surgeons (Drs. Gessner, Parham, Maes, Danna, Lafferty, and others) who have adopted the endoaneurysmal suture and successfully applied it in the treatment of arteriovenous lesions.

But I must proceed with the treatment of that most familiar type of arteriovenous injury, the *aneurysmal varix* or fistula, which has furnished me with the largest and most varied experience in nine cases, in all of which I have applied the principle of the endoaneurysmal suture in its restorative phases, with a success that could scarcely have been obtained by any one of the conservative or radical procedures in vogue.

In order to approach this subject more intelligently, a brief reference to the historical evolution of the special modification of the endoaneurysmal method, as adapted to the peculiarities of aneurysmal varices, is necessary.

Endoaneurysmal Suture by the Transvenous Route. In the *Annals of Surgery* for February, 1903, I published my first systematic ac-

count of the endoaneurysmal method of suture which I had first applied to a brachial aneurysm on March 30, 1888.[1]

My paper dealt with arterial aneurysms and not with arteriovenous lesions, though the indications for the suture in these cases were obvious. This gap in the technic, however, was quickly filled by my friend and former associate, Dr. W. S. Bickham of New York, who in an excellent paper published in the *Annals of Surgery* for May, 1904, suggested and elaborated a most ingenious technic for the application of the intrasaccular suture to the various lesions grouped together under the name of arteriovenous aneurysms.

The methods suggested and so clearly illustrated by Dr. Bickham in 1904 will be found more systematically described in his excellent "Text Book of Operative Surgery" (Third Edit., Saunders, 1908), under the heading of "Operations for the Radical Cure of Arteriovenous Aneurysms with Preservation of the Circulation in the Artery and Vein: (The Matas-Bickham Operation)."

Bickham's foresight and planning of this technic based upon the theoretical possibilities offered by the most familiar types of arteriovenous aneurysms is, indeed, most remarkable and praiseworthy.

The first clinical application of one of Bickham's suggestions, viz., to attack the problem of closing the fistula in aneurysmal varix by the *transvenous* route, was first demonstrated clinically by my friend and associate, Dr. H. B. Gessner, in the case of a colored laborer, age twenty-two years, who had sustained a gunshot injury (multiple small shot) in the abdomen and right thigh. The injury had been inflicted eleven years previously and involved the femoral vessels in Hunter's canal. The injury had caused comparatively little disturbance. The operation was performed on May 30, 1908. The sac itself was small, and notwithstanding the long duration of the injury, there were none of the varicosities or trophic changes in the skin of the lower extremity which characterize the progressive types of varix aneurysmaticus. The thrill and murmur caused the patient anxiety, and this was the chief reason for the intervention. In this case the sac was formed by ampullar dilatation of one of the venæ comites, the other being intact. Three arteriovenous fistulæ caused by small shot were discovered in the interior of the venous sac when this was opened. They were all closed by

[1] *Med. News*, Phila., October 27, 1888.

FIG. 1. CASE OF JOHN G. (Jugulo-carotid Aneurysm), OF FIFTEEN YEARS' STANDING.

Showing great plexus of tortuous, pulsating superficial veins in neck. Also puffiness of left face and corresponding exophthalmos.

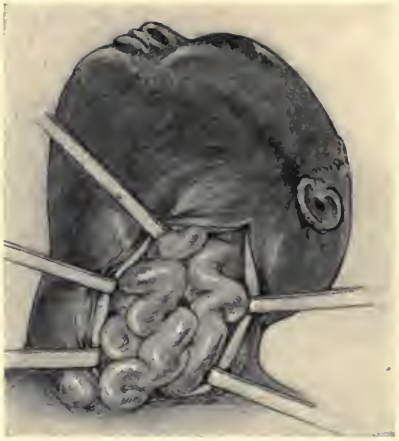

FIG. 2 (diagrammatic). Showing enormous dilatation and varicosities of superficial venous plexus after dissection. (Case of John G., Jugulo-carotid Aneurysm.)

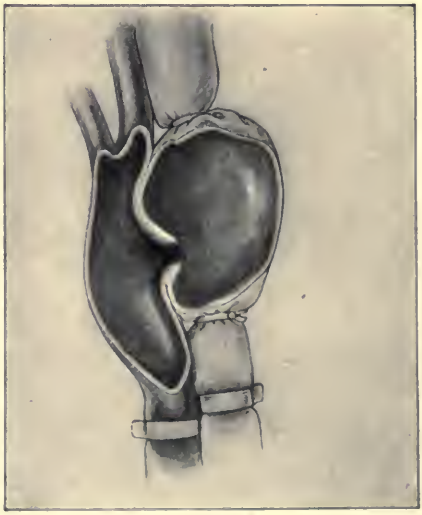

FIG. 3. CASE OF JOHN G. (Jugulo-carotid Aneurysm).

Showing the relations of the carotid and jugular. The septum separating the two vessels; the anastomotic communication. The aluminum bands applied to the artery and vein and the two additional ligatures on the vein above and below the arteriovenous fistula.

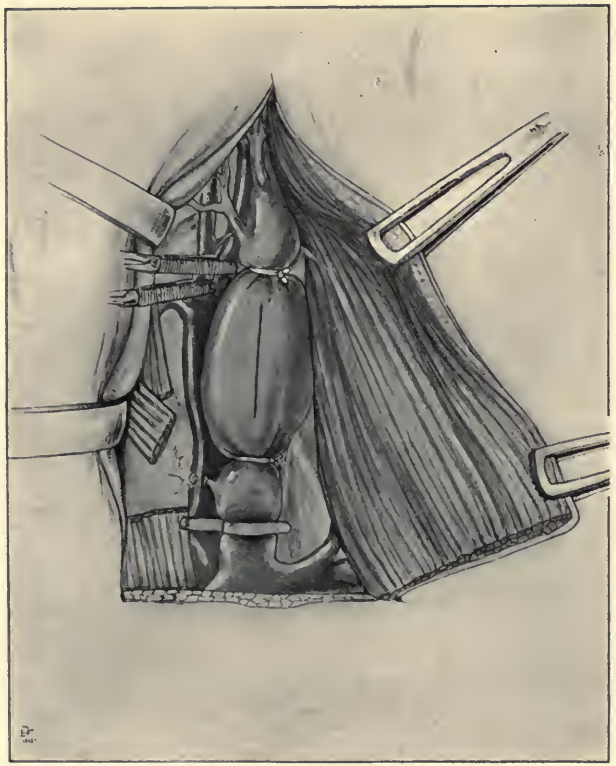

FIG. 4. DEEP DISSECTION AFTER CLEARING OUT SUPERFICIAL VENOUS PLEXUS.

The Internal Jugular Vein is Seen Resting upon the Common Carotid at Seat of Arteriovenous Anastomosis. An Aluminum Band has Been Placed upon the Common Carotid and on the Jugular on the Proximal Side of the Arteriovenous Communication. A Ligature has also Been Placed upon the Vein Nearer the Venous Sac on the Distal (Cephalic) Side. The External and Internal Carotid Arteries are Occluded Provisionally with Padded Clamps. The Line of Incision on the Venous Sac Indicates the Site of the Anastomosis. (John G., Jugulo-carotid Aneurysm.)

FIG. 5. CASE OF JOHN G. (Jugulo-carotid Aneurysm).

Shows the dilated vein opened after controlling the circulation in both vessels. The arteriovenous orifice exposed and first continued row of sutures (silk) applied.

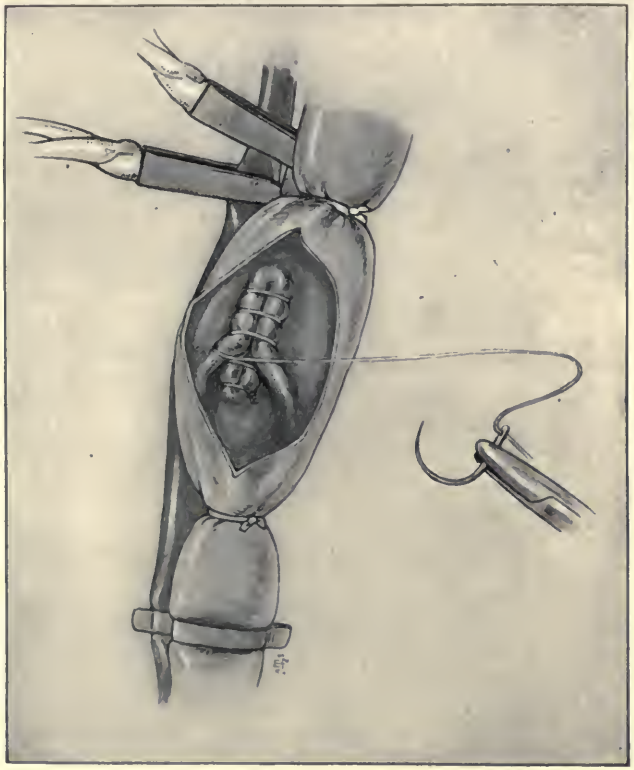

FIG. 6. CASE OF JOHN G. (Jugulo-carotid Aneurysm).

Shows fistula closed and second re-inforcing row of silk sutures applied through venous wall.

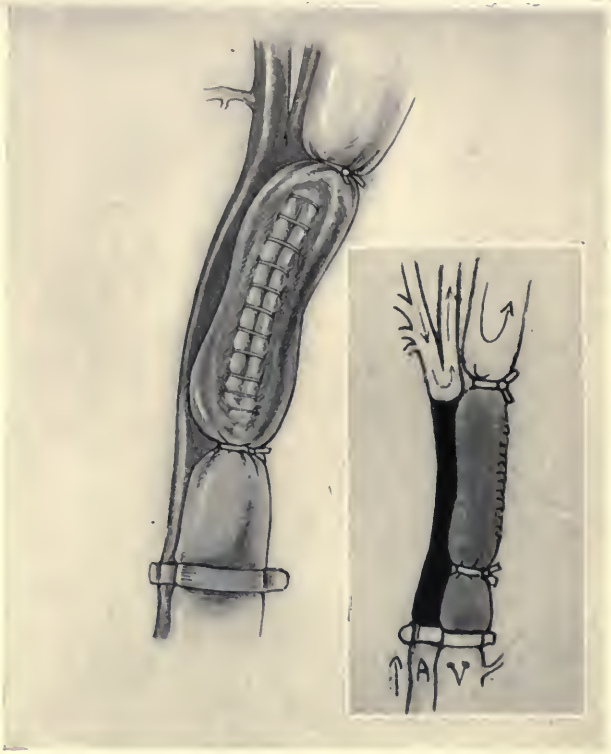

FIG. 7. SAC OBLITERATED AND CLOSED.
(John G., Jugulo-carotid Aneurysm.

All Circulation in the Vein Arrested between the Permanent Ligatures. Elastic Padded Clamps Removed from the External and Internal Carotid Arteries, thus Allowing a Reduced Collateral Circulation to Continue from the External to the Internal Carotid through the Bifurcation, in Spite of the Permanent Occluding Aluminum Band on the Carotid.

The Smaller Diagram Shows Areas of Possible Circulation in the Common Carotid and the Jugular at the Close of the Operation. The Black and Shaded Areas in the Artery and the Vein are Stagnant Areas; a Small Clear Strip Remains in the External Carotid and the Internal Carotid, Showing how Blood may Reach the Brain through the Bifurcation, even after the Obliteration of the Common Carotid.

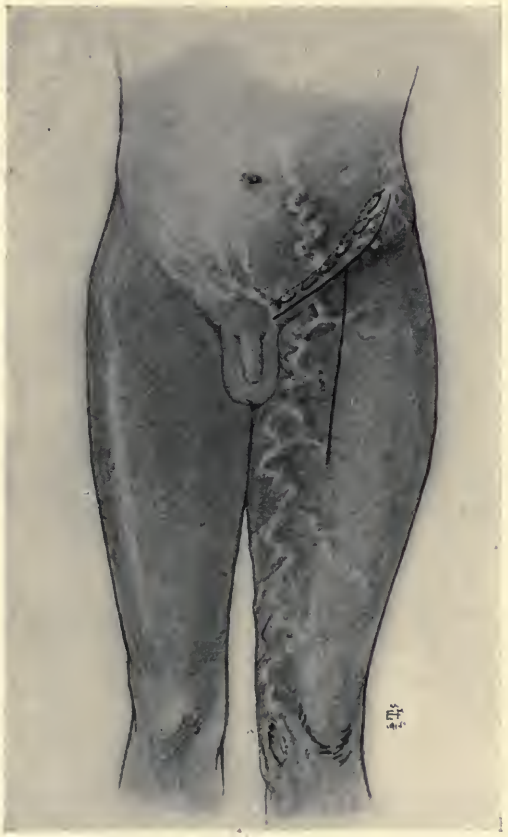

FIG. 9. CASE OF J. H. H. (Arteriovenous Aneurysm of the Common Femoral Vessels.)

External appearance of the left lower limb, showing Varicosities and Line of Incision, also Line of Continued Percutaneous Suture to Control Bleeding from Superficial Abdominal Plexus of Veins.

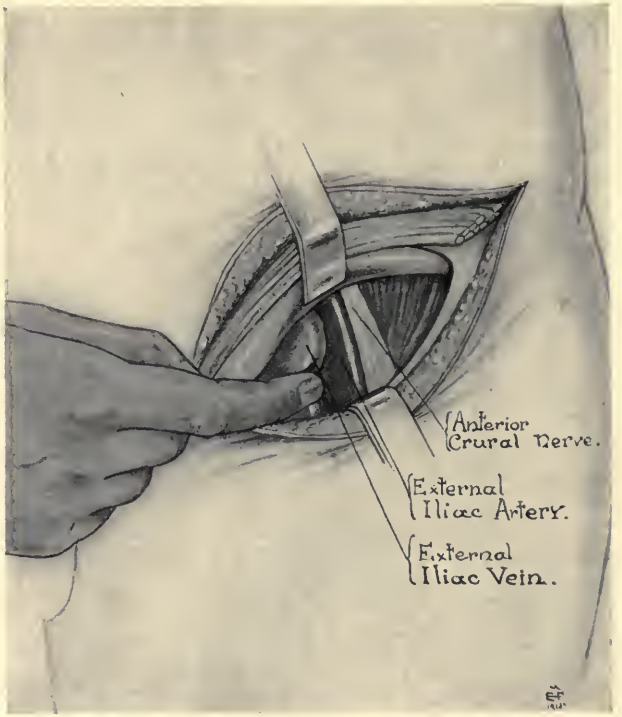

FIG. 10. CASE OF J. H. H. (Arteriovenous Aneurysm of the Common Femoral Vessels.)

Iliac Incision showing relations of External Iliac Vessels and Anterior Crural Nerve, the finger pushing the enormously dilated vein aside.

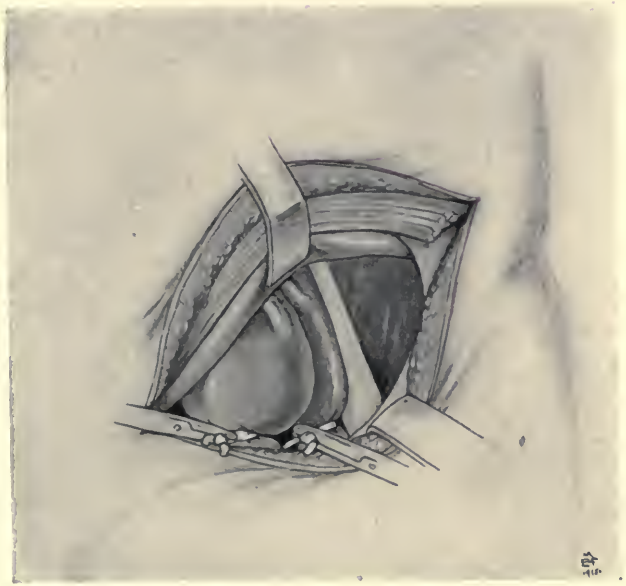

FIG. 11. CASE OF J. H. H. (Arteriovenous Aneurysm of the Common Femoral Vessels.) SAME DISSECTION SHOWING ARTERY CONTROLLED BY PROVISIONAL ELASTIC LIGATURES.

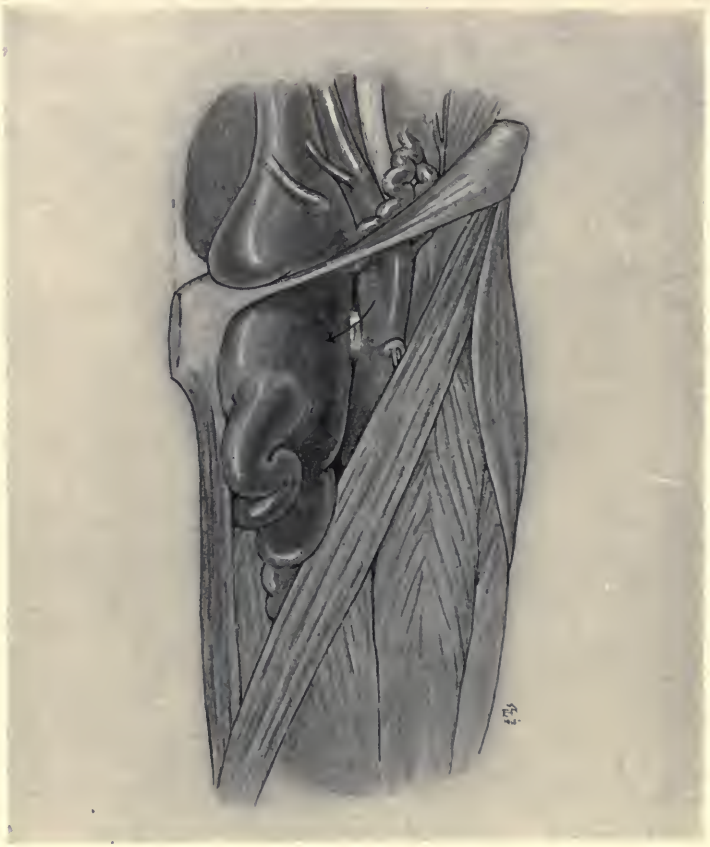

FIG. 12. CASE OF J. H. H (Arteriovenous Aneurysm of the Common Femoral Vessels.) APPEARANCE OF DISSECTION ABOVE AND BELOW POUPART'S LIGAMENT.

Shows Seat of the Arteriovenous Anastomosis and Enormous Enlargement of the Vein.

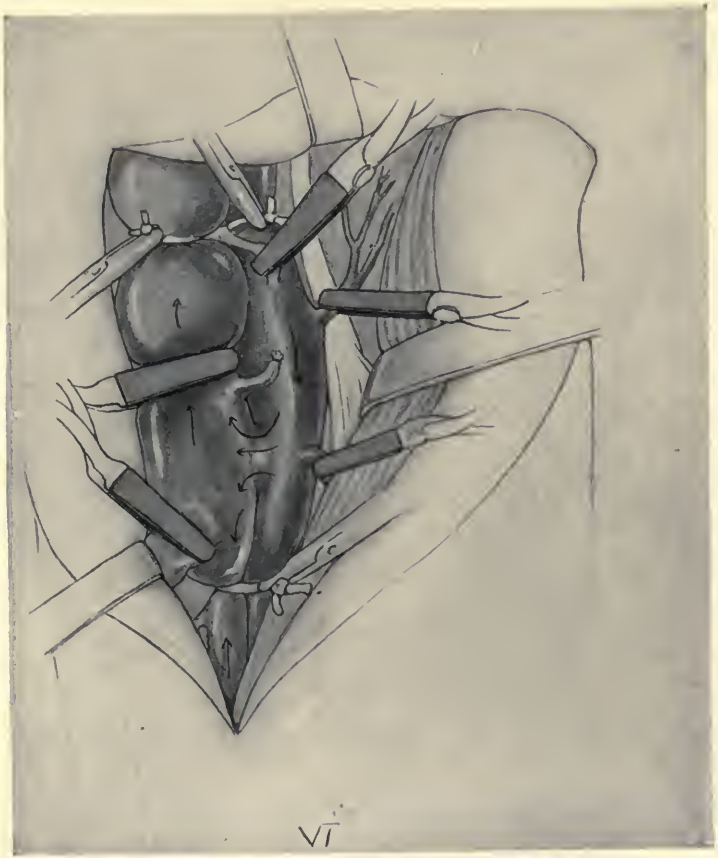

FIG. 13. CASE OF J. H. H. (Arteriovenous Aneurysm of the Common Femoral Vessels.) DEEP DISSECTION AFTER DIVISION OF POUPART'S LIGAMENT AND METHODS OF PROPHYLACTIC HEMOSTASIS BEFORE ATTEMPTING THE DETACHMENT AND SEPARATE SUTURE OF THE VESSELS.

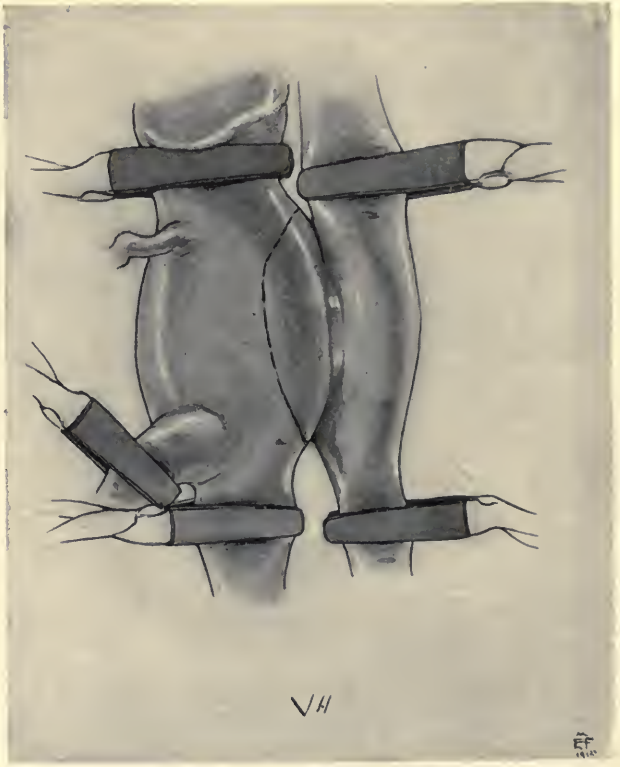

FIG. 14. CASE OF J. H. H. (Arteriovenous Aneurysm of the Common Femoral Vessels.) DETAIL OF ANASTOMOSIS TO SHOW LINE OF INCISION ON THE VEIN IN ORDER TO EXPOSE THE INTERIOR OF THE SAC.

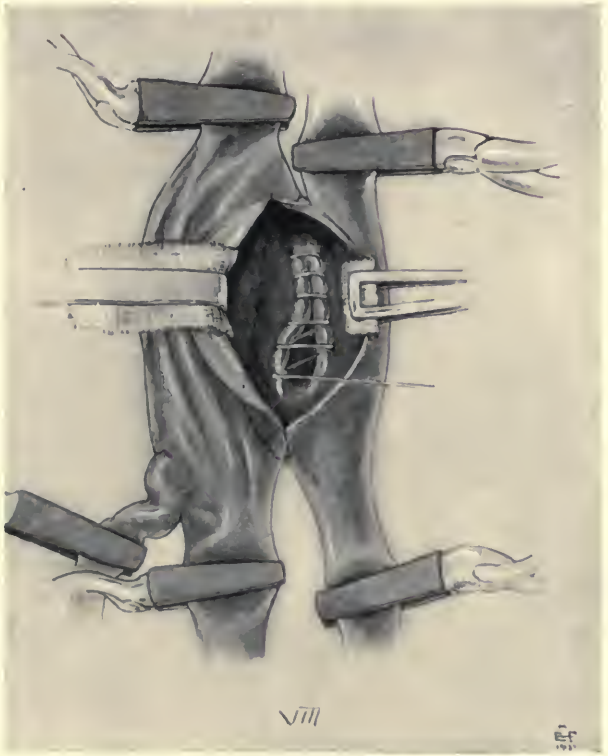

FIG. 15. CASE OF J. H. H. (Arteriovenous Aneurysm of the Common Femoral Vessels.) INTERIOR OF THE SAC, SHOWING CLOSURE OF THE ORIFICE OF COMMUNICATION BY CONTINUED SILK SUTURE.

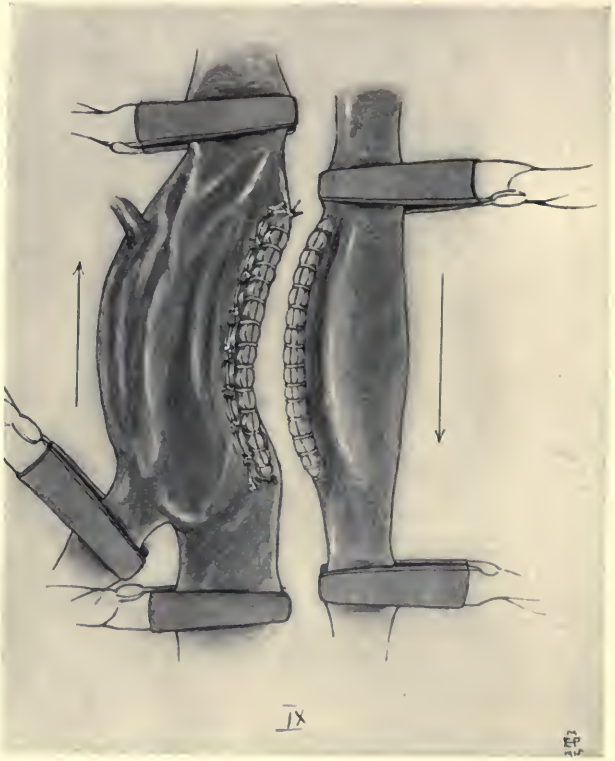

FIG. 16. CASE OF J. H. H. (Arteriovenous Aneurysm of the Common Femoral Vessels.) THE ANASTOMOSIS CLOSED; ARTERY AND VEIN DETACHED, ISOLATED AND SEPARATELY CLOSED BY LATERAL ARTERIO- AND PHLEBORRHAPHY.

The Arterial Orifice has been Closed Separately by Intrasaccular Suture on the Venous Side and the First Line of Intrasaccular Sutures is Reinforced at the Expense of the Vein.

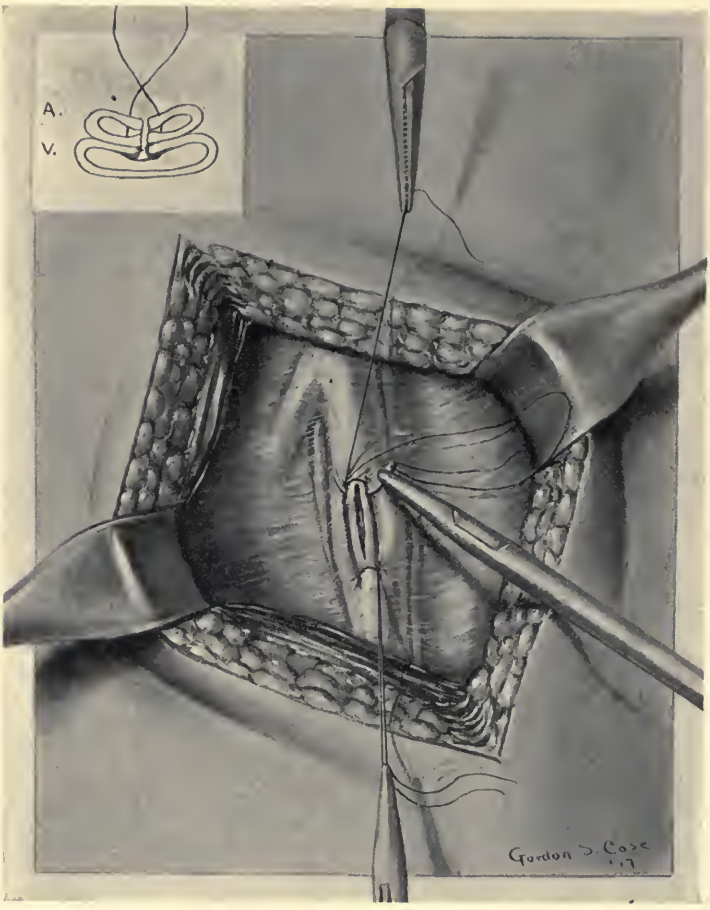

FIG. 18. Shows Interior of Large Space Occupied by Hematoma, Covered Over with a Veil of Semitranslucent Exudate in Process of Organization. (J. B. Arteriovenous Hematoma of Femoral Vessels.)

First Stage of the Suture. The Needle is shown Penetrating through Both Walls of the Artery and through the Arteriovenous Septum, so as to Close the Narrow Fistula which Connected Both Vessels. By Lifting the Walls of the Collapsed and Thin Vessels with Two Traction Sutures, one at each End, the Curved Needle was able to Penetrate the Septum and Obliterate the Orifice in the Vein, and in the Artery, without Obliterating the Lumen of the Vein and only Partially that of the Artery. The Method of Closure by Suture is Shown in the Insert A and B.

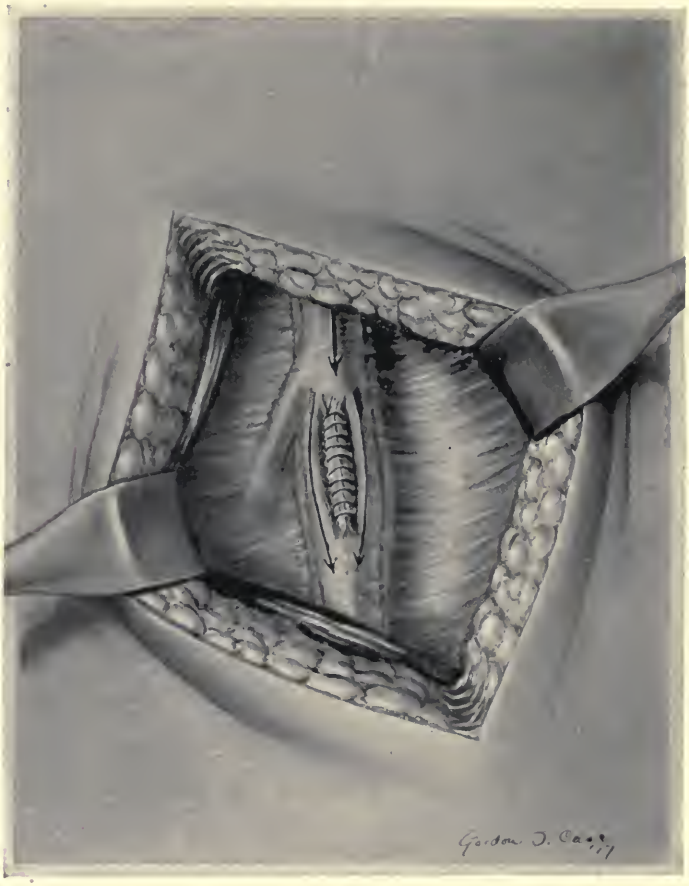

FIG. 19. SHOWS THE RESULT OF THE SUTURE (PARAFFINED SILK).

(J. B. Arteriovenous Hematoma of Femoral Vessels.)

The Suture Closed the Fistula and Allowed Blood to Circulate through two Narrow Channels, on Each Side of the Line of Suture. The Artery Pulsated very Distinctly *after* Total Suppression of the Thrill and Other Signs of Arteriovenous Fistula had been Obtained. The Sac of the Hematoma was Obliterated by Allowing the Sartorius to Fill the Space after Clearing out the Clot. Healing *per Primam* and Perfect Recovery.

separate intrasaccular sutures and the artery left undisturbed. The sac itself was infolded and obliterated by suture.

The next case came under my observation in 1912 and gave me the opportunity to apply, for the first time, Bickham's suggestion of the *transvenous* route as a means of approach to an arteriovenous fistula in a typical aneurysmal varix of the jugulo-carotid tracts of long standing. It was a most difficult and forbidding case, and I do not see how I could have accomplished what I did by any other method.

Arteriovenous Fistula (Gunshot of Fifteen Years' Standing) of the Jugulo-carotid Tracts, at the Bifurcation. Obliteration of the Orifice of Communication by Direct Suture Applied by the Transvenous (Transjugular) Route, Leaving an Open Collateral Channel to the Brain via the External and Internal Carotids and the Bifurcation. (See Fig. 1.) The patient, John G., an intelligent negro barber, age forty years, consulted me first on April 12, 1912. He had been shot in the neck fifteen years before he applied to me for relief of symptoms caused by an aneurysmal varix which, in the course of these years, had led to an enormous dilatation of the jugular and all the tributary veins. The man had been shot in an altercation, with a revolver, at close range, and the bullet (.38 caliber) had perforated the internal jugular and the common carotid on a level with the bifurcation. The bullet, as was discovered fifteen years after, had lodged in the back of the neck and could be seen, in the radiograph, behind the articular process of the third cervical vertebra. The hospital record shows that one hour after the injury he developed unmistakable signs of an arteriovenous communication, which persisted and gradually grew worse as time went on. Simultaneously with the bivascular injury, the spinal cord had been wounded. From this injury he gradually recovered in the course of five years. Also, as an immediate sequel of this injury, he developed a traumatic meningitis, with hyperpyrexia (107.6°) which kept him in a state of unconsciousness and delirium for fifteen days. He recovered slowly, but was finally discharged from the hospital, hemiplegic, with the aneurysmal varix in full activity. Apart from the annoying thrill and great noises which he heard roaring in his head, he was fairly comfortable and was able, at the end of five years, to return to his trade as barber. It was not until about one year before his consultation with me that the aneurysm, or, at least, the swelling in his neck, grew rapidly, and he began to suffer with dyspnea and with "choking spells" whenever he made unusual muscular efforts. He then had to give up his work and go to bed. His history also showed that he had been a steady drinker and a syphilitic. He had a large dilated heart

and aorta with an aortic obstructive murmur, an irregular pulse, and relatively low blood pressure. He was a stout man, weighing over 212 pounds, and his neck was disproportionately large from the great turgescence and enormous dilatation and tortuosity of the superficial veins, which pulsated, purred, and thrilled like living things. He had also developed a left-sided exophthalmos caused by the dilatation of the retrobulbar veins, which gave him a very striking appearance.

Whenever he exerted himself he was seized with dyspnea and a great anxiety, which he attributed to the aneurysm, as the veins swelled and formed a collar which, he said, "strangled him."

At first, I would not consider an operation, because I believed the cardiovascular lesions were so advanced that they would soon prove fatal. However, after observing him for one month, it occurred to me that the dyspneic spells were, in part, due to the great strain imposed upon the right heart by the constant inflow of the enormous stream of arterial blood which was being short-circuited from the arterial into the venous system, through the fistula, at the abnormal jugulo-carotid junction. For nearly fifteen years his heart had been able to stand the strain by compensatory hypertrophy; but now, in consequence of myocardial degenerative changes, it yielded to the strain at the slightest provocation, and he was in constant danger of an acute dilatation. It seemed to me that if the fistula could be closed, the great strain on the heart would be relieved and his general condition improved. Chiefly for this reason I yielded to his urgent solicitation, but with grave misgivings as to the outcome, which he fully realized.

The Operation. I decided that I would operate in two stages. The first was to be limited to the clearing out of the great mass of superficial veins which were in the way and prevented a free access to the common carotid; then, a removable aluminum band, of the type that we had been using for years for this purpose (Matas-Allen band), was to be placed on the artery with a view of testing the efficiency of the collateral circulation in the brain, through the circle of Willis. The first stage was to end with this step, the wound was to be closed, and the effect of the carotid occlusion on the brain was to be observed for several days. If no complications followed, the second stage was to be undertaken in a few days with a view of closing the arteriovenous fistula and curing the aneurysm. This program was carried out to the letter, with some additions, on May 4, 1912. In view of the great dangers of general anesthesia, the operation, in two stages, was performed under local and regional anesthesia with novocain-adrenalin solution, preceded by a hypodermic of morphia gr. 1/4 and scopolamin gr. 1/150.

The difficulties of the operation were just as great as we had antici-

pated and, in completing its first stage, two hours and a half were consumed in one of the most difficult, tedious, and trying dissections that I can remember in all my surgical experience. We were greatly assisted, however, by the patient's stoic and even cheerful attitude. He never complained and helped us at all times by placing his head and neck in the most favorable position for our work. In this way we were able to clear the field of the immense pulsating and squirming plexus of the veins which covered the entire field from the submaxillary region to the sternum and clavicle, with very little loss of blood and with all the deliberation and neatness of a cadaveric dissection. (Fig. 2.) When this had been done the sternomastoid was divided at its sternal and clavicular attachments and reflected outwards, thereby exposing an immensely dilated jugular which completely overlapped and covered the carotid. (Fig. 4.) After dividing the omohyoid and sternohyoid, the site of the anastomosis was easily recognized as a cicatricial plug, which could be felt over the mass that bound the carotid and jugular with the sheath of the vessels and held them together in an inextricable, fused, pulsating mass. Pressure at this point, which was the vortex of the great circulatory storm that raged in these parts, put an immediate stop to all pulsation and brought about the collapse of the veins. We availed ourselves of this subsidence in the venous swelling to clear out the common carotid and apply the aluminum band on this trunk at about 1½ inches above the left sternoclavicular joint. The seat of the anastomosis we had now located, with accurate precision, on a level with the bifurcation. On releasing the pressure at this point, the jugular filled again and pulsated, but very much less vigorously than before the banding of the carotid. In view of this greatly diminished activity of the arteriovenous circuit, an additional band was placed on the jugular about 1 inch from its junction with the subclavian. Seeing now that the vein became distended and pulsated to the level of the obstruction, a chromic catgut ligature was placed on the vein 1½ inches higher up, and that much nearer to the anastomosis. This reduced the size of the ampullar swelling very considerably; and, as the first stage of the operation had been completed, we decided to close the wound provisionally.

Notwithstanding the long and tedious ordeal, the patient was sent back to his bed in excellent condition, with a pulse of 100, respirations 22, and in a cheerful frame of mind.

In the absence of all complications, cerebral or otherwise, the second stage of the operation was undertaken on the third day after the first operation, when the dressing was removed for the first time.

Second stage. On lifting the cutaneous flap the wound was found clean. The occlusion of the carotid and internal jugular had exercised a wonderful

influence in diminishing the venous turgescence and erethism of the whole field of the operation. One significant fact remained—the arteriovenous fistula at the carotid bifurcation was still active. The pulsation and thrill could be still felt at this point, though greatly subdued. It was evident that the arteriovenous fistula was now fed by the arterial current which was coming from the collaterals of the opposite side through the external carotid to the internal carotid and again into the jugular through the fistula. (See Fig. 3.) Evidently, the flow into the jugulo-carotid fistula could not be stopped, or the aneurysm cured, until the circulation going on through the external and internal carotids had been arrested. To accomplish this, these vessels were temporarily and individually compressed above their origin at the bifurcation with two small, padded Hoepfner clamps. (See Fig. 3.) The internal jugular was now ligated on the cephalic side of the arteriovenous junction. This made it safe to proceed with the next step of the operation, which was to open the jugular vein freely over the site of the fistula and thus expose the interior of its ampullar swelling and close the orifice of communication leading to the artery through the venous side. A longitudinal incision of about 2 inches was made into the venous pouch through its collapsed walls. The orifice of the fistula was now brought to view. It was elongated, oval shaped, and half an inch in its longest diameter. Beyond it, the lumen of the enlarged carotid could be recognized, and by passing a vaselined probe the orifices of the internal and external carotids could be felt arising a short distance beyond the edge of the opening. The opening itself seemed to occupy the center of a partition or diaphragm, formed by the adherent walls of the artery and vein. There was no interposed space or sac between the two. The edges of the fistulous orifice were smooth and rounded, and just thick enough to give a good, firm grip to the small curved needle and paraffined silk that was used to close it. Six continued sutures, passed through the edges of the opening, were quite sufficient to close it hermetically. (See Fig. 5.) To secure further protection, a second line of continued chromic gut suture was made to cover the first line, by plicating the relaxed venous walls over it. (See Fig. 6.) This reduced the cavity of the venous sac to a notable extent, but still left a very considerable excess of sac, which was partially trimmed off with scissors—sufficiently to permit the complete obliteration of the cavity by infolding the edges of the vein and holding them in apposition ("capitonnage") by a continued gut suture. In this way what was once a large venous ampulla was transformed into a thick padded cord which completely obliterated the jugular from the proximal to the distal ligatures which had been previously placed on the vein, above and below the anastomosis. (See Fig. 7.) The clamps were now removed from the external and internal carotids. It was soon de-

termined that a reduced circulation had been established through these vessels, by way of the bifurcation, and that while the arteriovenous communication had been completely closed, a new channel for the arterial supply of the brain had remained. In this way, also, the main object of the operation had been obtained with the sacrifice of the vein, but with a greater conservative result on the arterial side than we had anticipated. This second sitting consumed, in all, about 1½ hours, and was also carried out without any general anesthetic, except a preliminary hypodermic of morphia and scopolamin. At the close, the wound was carefully dressed and drained at the lower angle.

All signs of the arteriovenous anastomosis had disappeared completely. From May 6th to 8th the patient continued to do well, only complaining of pain in swallowing. On dressing the wound on the 8th, evidences of suppuration and staphylococcal infection were discovered in the tract of the drain, and several sutures were removed, allowing some seropurulent fluid to escape. The infection had begun under the flap, and a cellulitis was suspected between the lower carotid sheath and the pharynx. The pulse rose to 100° and showed more irregularity and intermittency. The mental attitude was perfectly clear and even cheerful; no evidences of cerebral disturbances. Dysphagia and occasional spells of dyspnea were the chief troubles. The wound was dressed twice daily, and the infection seemed to be controlled. On the night of the 11th he became restless and anxious, and complained that he could not breathe comfortably and had to be propped up on pillows. On the morning of the 12th he washed his mouth and attended to his toilet as usual, but persisted in sitting up. At 8.30 A.M. he complained of stenocardiac pains and distress in the precordia, and began to struggle for breath. The pulse now became very irregular and feeble and he expired suddenly before the interne of the service could reach him.

Death, therefore, occurred nine days after the first operation, when the carotid and jugular were occluded, and on the sixth day after the second sitting, when the arteriovenous fistula was obliterated.

At the autopsy, nothing was found in the wound that could account for the fatal termination. The fistula had been completely sealed and all the sutures had held. The internal and external carotids were pervious and free from clot. The brain and thoracic organs were preserved for a separate and detailed examination in the laboratory. Marked evidence of chronic endarteritis and miliary aneurysms were discovered in the cerebral vessels, but the cause of the fatal termination was found in the heart. The aorta was dilated and showed atheromatous plaques. The left coronary was obstructed by thrombus and the right ventricle was distended with clot which extended into the pulmonary artery. The heart itself was of large size, dilated, showing evidence of myocardial degeneration.

I have dwelt with some detail upon the report of this patient's case, because it presents many unusual, if not unique, features:

1. It is the first case that I have been able to discover in the literature in which the special technic of transvenous endoaneurysmoraphy has been applied to suppress an arteriovenous fistula of the jugulo-carotid vessels, with technical success. The only other instances in which the *transvenous* method of endoaneurysmal suture has been applied are reported six years later, and are: (1) the operation performed on a young soldier by René Le Fort, of Lille, on July 20, 1917[2] in which the *internal* carotid and jugular veins were involved. The fistulous communication was closed by suture, applied through an incision made in the pouch formed by the dilated internal jugular. The artery remained pervious, and the vein was obliterated by plication and mattress sutures ("capitonnage"), as in my case. The wound had been inflicted four months previously, and the technic was remarkable for its simplicity and brilliant success.

(2) The operation reported by C. P. Lecène of Paris[3] was performed on November 15, 1917. The patient, a soldier, aged twenty-five years, was wounded in the neck by a fragment of shell which perforated the common carotid and jugular, causing an arteriovenous anastomosis. The operation was performed about one month after the injury. In this, as in my case and Le Fort's, the jugular vein was enormously dilated on a level with the arterial communication. The operator was able to close the slit-like opening of the fistula, which was clearly visible inside of the vein, by an intravenous suture with fine silk, and, in this way, he did a perfect restorative endoaneurysmoraphy, which allowed the common carotid to remain pervious. The vein itself was closed by intravenous sutures applied above and below the seat of the anastomosis. The result was a brilliant success, by which the carotid circulation was restored, though the vein was partially obliterated.

This case, as the preceding of Le Fort, is noteworthy in many ways, and especially as illustrating the relative facility with which the cure of an aneurysmal varix was effected in a particularly dangerous and difficult region. It is also a valuable tribute to the efficiency of the method, coming, as it does, from an operator who

[2] *Bull. Acad. de Méd., Par.*, No. 31, August 7, 1917.
[3] *Bull. et mém. Soc. de chir. de Par.*, January 15, 1918; XLIV, No. 1, 27-30.

had previously entertained, and expressed, a decided prejudice against the endoaneurysmal methods of suture, but who, after this experience, loyally and honestly admitted that he had erred in his preconceived objections.

"Mais l'expérience qui seule juge en dernier ressort, m'a montré que mes préventions contre cette intervention (l'opération de Matas) étaient tout a fait injustifiées."

2. In our case the continuity of the collateral arterial current to the brain through the external and internal carotids by way of the bifurcation remained undisturbed, and is also one of the unique features of this case. The proof that this collateral circuit remained active was demonstrated after the common carotid and internal jugular had been occluded.

3. The chief indication for the operation was also unusual, and perhaps unique, in the fact that it was undertaken chiefly with the hope that the closure of the arteriovenous fistula would relieve the strain on the right heart caused by the short-circuiting of the carotid stream into the venous system, causing a progressive dilatation, with dangerous and distressing symptoms.

The opportunity to test the full value and end results of the transvenous route in attacking aneurysmal varices, which was denied us in the preceding case, soon presented itself in a succession of aneurysmal varices of the lower extremities, which came under treatment in our clinics in the interval between 1912 and 1919. The following two cases, abstracted from our records, suffice to show some of the peculiarities of the technic, which has varied according to the conditions found in each case, but has always been guided by the same principle.

Traumatic Arteriovenous Aneurysm (Aneurysmal Varix), Involving the Femoral Vessels at the Groin, of Three Years' Standing in which the Arteriovenous Communication was Successfully Closed by Transvenous Endoaneurysmorapby, with Preservation of the Lumina of Both Vessels. The patient, J. H. H., nineteen years, of Westminster, S. C., shot himself accidentally with a parlor rifle, .22-caliber bullet. The bullet entered the abdominal wall about 1½ inches below Poupart's ligament, and ranged downward, striking the femoral vessels at the groin, and losing itself in the depths of the left thigh. A tumor formed just below the middle of Poupart's ligament, where a characteristic thrill and purring noise developed on the

third day following the injury. He came under my observation on January 11, 1912, *three years* after the accident occurred. The affected limb was larger than the right, and he had large varicosities all along the saphenous tract from the thigh to the leg, with typical pigmentation of the skin and a rebellious ulcer below the knee which had resisted all previous treatment. The site of the abnormal vascular communication was easily localized at a point just below Poupart's ligament, a little to the inner side of the mid line. At this point, the pulsation, thrill, and characteristic murmurs were heard with greatest intensity. From this point the murmurs and thrill were transmitted upward as far as the umbilicus and, below, as far as the knee. The details of the operation which followed are well shown in the accompanying diagrams and drawings. The iliac vessels were exposed by an extensive subperitoneal dissection, great difficulty being experienced in controlling the external iliac vein and its tributaries, which had attained enormous proportions. The iliac vessels were provisionally controlled above and below the anastomosis (after Poupart's ligament had been divided) by elastic ligatures and padded clamps. The common femoral veins formed a large, well-defined sac of egg-like shape at the site of the fistula at its junction with the saphenous. After controlling all the vessels, the aneurysmal phenomena were all stilled and the vessels collapsed. The sac, which was fully 3½ inches in length and 2 inches in breadth, had developed between the artery and the vein, but at the expense of the vein. The constriction or neck which united the sac with the artery was fully 1½ inches in length. The sac was opened longitudinally on the venous side, exposing

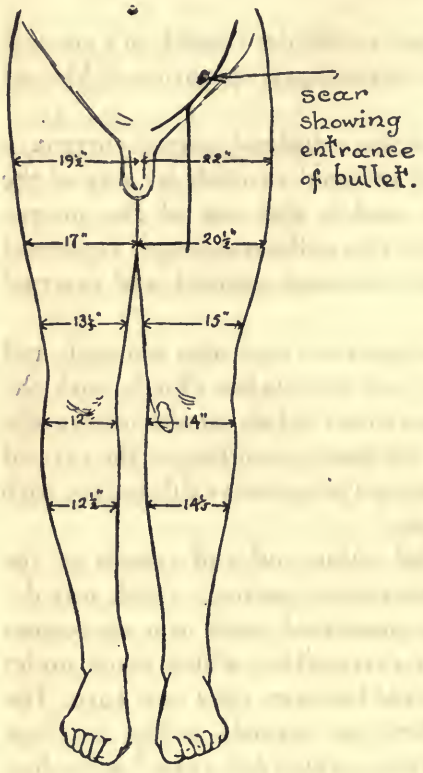

FIG. 8. CASE OF J. H. H. (ARTERIOVENOUS ANEURYSM OF THE COMMON FEMORAL VESSELS)

SHOWING COMPARATIVE MEASUREMENTS OF THE LOWER EXTREMITIES; SWELLING CAUSED BY VARICOSITIES AND EDEMA; ALSO ULCER BELOW KNEE AND LINE OF INCISION, AND SCAR SHOWING ENTRANCE OF BULLET.

the full length of the large orifice in the artery. This was closed by a row of continued, vaselined silk sutures introduced from the venous side, thus bringing the endothelial surfaces of the orifices in perfect apposition. After this, a cuff flap was cut off at the expense of the venous wall, thus detaching the artery completely from the vein. This flap was sutured over the cuff in the manner shown in the diagram, leaving the artery thoroughly protected against leakage. The suture of the vein was easily accomplished, owing to the excess and laxity of the venous sac. After this, all the controlling elastic ligatures and clamps were removed, allowing the blood stream to return at once through its normal channel. All the sutures in the artery and vein held perfectly, insuring the complete success of the operation. The operation was long and tedious, as was to be expected in such a chronic case, lasting nearly four hours. This was due chiefly to the innumerable and enormously dilated veins which had to be secured and extirpated in the superficial planes before the main vessels could be reached. (See Figs. 9–16).

The most notable post-operative feature of the case was the extraordinary tachycardia that developed suddenly after the restoration of the circulation through its normal channels. This tachycardia, during which the pulse ranged from 170 to 190, continued until after the patient had recovered from the anesthesia, and lasted for three hours after he was returned to his bed. At the end of this time the pulse suddenly became irregular and dropped in three minutes to 110, where it continued until it became normal the next day. Apart from this remarkable incident the patient made an excellent recovery and was discharged completely healed and well, on February 19, 1912. Three years after his return home his physician wrote me that the boy had been in perfect health and that he had grown to be a big and robust man.

In this case, as in all others of long standing, the baneful effects of the short-circuiting of the large arterial channels, into the venous circulation, especially at the root of the limbs, were particularly noticeable, showing that the sudden readjustment of the circulation by the closure of the abnormal arteriovenous communication is not without its dangers.

Arteriovenous Aneurysm of the Femoral Vessels at the Apex of Scarpa's Triangle in a Boy of Fifteen Years in which the Orifice of Communication was Closed by a Trans-arterial Suture. A pulsating hematoma caused by the simultaneous transfixion of the artery and puncture of the vein by stab. (See Fig. 17.) This boy, J. B., was brought to me from Sterling City, Texas,

September 3, 1916, twenty-four days after he had accidentally wounded himself in the right thigh with a long-bladed pocket knife, while splitting a piece of wood. The knife had entered the upper thigh about 5 inches below Poupart's ligament. The boy was still suffering from the effects of severe hemorrhage. A linear scar indicated the point of entrance of the knife, and about this was a spherical swelling which pulsated, purred, and thrilled in the characteristic fashion of arteriovenous injuries. The pedal pulses were feeble, but, on testing the collateral circulation by our methods, it was shown that an ample supply of blood was going to the periphery by the collaterals outside of the main channels, and that an obliterative operation could be performed with safety, if it became necessary. Prophylactic hemostasis was secured by the Esmarch bandage, and the constrictor was held high up near the groin with a Wyeth pin. With the scar as the center of the incision, a sac was opened above the sartorius, which led to another cavity under this muscle. This cavity was already partially lined with a thin veil of organized exudates which hid the vessels completely. A slit-like opening about half an inch in length was now discovered in the floor of this space, running parallel with the long axis of the femoral vessels, which were lying superimposed one on the other under the thin lining of the sac. An exploration of this opening with a probe demonstrated that it led to the artery and not the vein, as we had at first supposed, and that this vessel had been transfixed and the vein punctured.

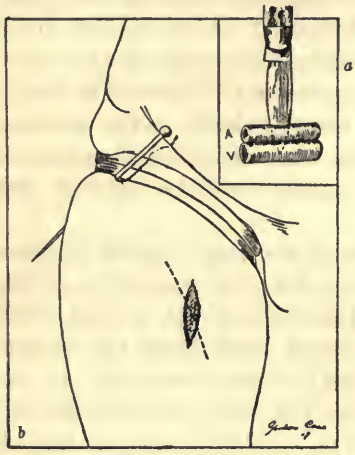

FIG. 17. Case of J. B. (Arteriovenous Hematoma of femoral vessels.) *a*. Shows How Penetration of Both Vessels was Made with Penknife; *b*. Portion of Scar where Thrill and Other Aneurysmal Signs were Most Marked; also Prophylactic Hemostasis with Constricting Elastic Band Held in Place by Wyeth Pin.

The flatness and breadth, as well as thinness of the collapsed artery, with the narrow slit-like wound lying in its center, permitted us to suture and obliterate the arteriovenous opening simultaneously with the external wound in the artery. The technic adopted is shown in the accompanying Figs. 18 and 19. On removal of the constrictor the blood rushed into the artery, which pulsated, circulating on each side of the suture line, and beyond, into the artery, distal to the central line of suture. All the aneurysmal signs ceased completely and the circulation of the foot was perfect, the pedal pulses remaining as they had been before the operation. Healing took

place *per primam*, and, after a short period of rest, hydrotherapy, and massage the patient was discharged, healed and well, on the twentieth day after the operation. I have since frequently heard from the patient, and up to the present time he is in perfect health.

This operation is unusual and perhaps unique in the fact that an arteriovenous fistula was obliterated through an abnormally thin arterial wall, thus constituting a trans-arterio-phleboraphy rather than the usual procedure of trans-phlebo-arterioraphy.

Our records show that four additional cases of arteriovenous aneurysms involving the femoral vessels have been operated upon in our clinics since going through the preceding experiences, which exhibit individual features and peculiarities of special interest to the surgical technician that deserve detailed consideration in a separate publication. They all have the one feature in common, in that they were long-standing aneurysmal varices presenting all the difficulties and complications peculiar to the chronic stages of this class of lesions, each one offering a serious problem to tax the judgment, skill, and resourcefulness of the most experienced operator. All of these, however, were happily solved by the intrasaccular and transvenous methods herein described, with such modifications as were suggested by the conditions met in the course of the operation. Finally, the experience gathered from these cases has convinced me that the possibilities of cure by this method are as great in arteriovenous aneurysms as in the purely arterial.

BIBLIOGRAPHY—SIR WM. OSLER'S WRITINGS ON ANEURYSM

[Perhaps no better illustration of Sir William Osler's broad catholicity of spirit and profound interest in every influence that tends to the uplift of medicine in all its relations, could be offered, than in his keen appreciation and penetrating insight into the borderland problems of vascular surgery. His numerous contributions to the knowledge and literature of vascular diseases, and especially aneurysm, even to the most surgical of these, arteriovenous injuries (incompletely represented in this bibliography), reveal the same accuracy of observation, the same capacity to collect, analyze, and interpret facts, the far-reaching clearness of the philosopher and erudite scholar that characterize all his writings in every department of thought which he has touched with the magic of his pen and illumined with his genius.—R. M.]

Geo. Ross and W. Osler, "Case of Aneurysm of the Hepatic Artery with Multiple Abscesses of the Liver," *Canad. J. M. & S.*, 1877–78, VI, 1.

W. Osler, "Case of Arteriovenous Aneurysm of the Axillary Artery and Vein of Fourteen Years' Duration," *Ann. Surg.*, 1893, XVII, 37.

W. Osler, "Notes on Aneurysm," *J. Am. M. Ass.*, 1902, XXXVIII, 1483.
W. Osler, "Aneurysm of the Descending Thoracic Aorta," *Internat. Clin.*, 1903, Ser. XIII, Vol. I, p. 1.
W. Osler, "Aneurysm of the Arch of the Aorta and Innominate," *Johns Hopkins Hosp. Bull.*, 1904, XV, 66.
W. Osler, "Aneurysm of the Abdominal Aorta," *Lancet*, October 14, 1905, II, 1089.
W. Osler, "Angina Pectoris, as an Early Symptom in Aneurysm of the Aorta," *Med. Chron.*, May, 1906, XI, 69.
W. Osler, "Aneurysm," in Clifford Allbutt and Humphry Davy Rolleston's "System of Medicine by Many Writers," VI; "Diseases of the Heart and Blood Vessels," 1909, 620–681.
W. Osler, "Aneurysms": "Aneurysm of the Thoracic Aorta; Aneurysm of Abdominal Aorta; Aneurysm of the Branches of the Abdominal Aorta; Arteriovenous Aneurysms—Aneurysmal Varix." Section IX, "Diseases of the Circulatory System," in "The Principles and Practice of Medicine," Eighth Edition, 1916, 847–861.
W. Osler, "Remarks on Arteriovenous Aneurysm." (Symposium on the subject at Radcliffe Infirmary, Oxford, March 26, 1915.) *Lancet*, London, May 8, 1915.

EXSTROPHY OF THE BLADDER

By C. H. Mayo, M.D., Rochester, Minn.

OF the many human defects none is more serious or troublesome to contend with than the condition of exstrophy of the bladder. It occurs, according to Spooner, four times in 116,000 births; according to Neudörfer once in 50,000 births, and since 1896 it has been observed in 52 instances in the routine examination of patients in the Mayo Clinic. The reason for the occurrence of this as well as of other anomalies has not as yet been satisfactorily explained. It has been shown experimentally, however, that defects of development may follow changes in the salts of the fluid which surrounds the developing egg.

The seriousness of the condition of exstrophy of the bladder hardly needs to be commented on. Statistics show that 50 per cent of all persons thus afflicted are dead by their tenth year, and 66.67 per cent are dead by their twentieth year. Other defects are often associated with it, such as hydrocephalus, spina bifida, hare-lip, imperforate or paretic anus, with rectal prolapse, and epispadias, which is usually present in the male, in whom 80 per cent of these cases are found. In the female the clitoris and labium minora are divided. In all cases the pubic arch is incomplete anteriorly, and separated for from 2 to 4 inches. Hernia, congenital or acquired, of one or both sides, is often an accompanying defect, and occasionally an umbilical protrusion is seen adjoining the upper margin of the bladder. The pelvis is broader and flatter than normal, a deformity which turns the femurs outward and produces, in extreme conditions, a curious wabbling gait. The umbilicus is situated lower on the abdomen than is usual; it is scarcely noticeable as it joins the upper bladder mucosa, thus showing that the defect occurs at the early period when the allantois is present. As there is no urachus the separation may extend from the cord juncture to the terminus of the urethra. Cases have been reported in which a normal urethra was present; this makes it improbable that obstruction and rupture could be a causative factor in its production (Duncan, 1805). The

period of development probably occurs when the pubic bone is still separated; one case is reported, however, of a child of five years with exstrophy of the bladder, the result of an assault, in which the pubic bones, originally joined, were later absorbed. The exposure and irritation of the bladder surface and the odor of leaking urine from the saturated absorbent cloths produce a most distressing condition, and lead persons thus affected to shun society; in fact unless an early operation is done, very few will have school advantages (Fig. 1).

Procreation in the male with this defect has not been reported. Winslow in 1906 reported one case of a woman who had borne four children, and Moorhead in 1916 reported one case of a woman who had borne two children. One of our patients, operated on by the plastic method, died later in childbirth; the baby weighed 12½ pounds. In the females with this defect whom we have seen, the vagina, uterus, ovaries, and tubes were normal, except in one case of bifid uterus and double vagina.

Deaths incident to the anomaly are usually due to nephritis, which may occur early from infection, or following a contracture of the lower ends of the ureter because of thickening of the bladder wall, which causes hydro-ureter and hydro-nephrosis. Later this becomes a pyonephrosis, but the infection does not necessarily travel through the lymphatic system of the ureter, as noted by Sweet and Stewart.

The difficulties of developing control of the urine in a receptacle formed from the remaining bladder tissue were early appreciated by scientific investigators. With the idea of bringing about a cloacal condition as common to birds, the ureters were transplanted into the intestine. This was first done unsuccessfully in 1851 by Simon. In 1852 Roux developed special plastic procedures for the formation of a bladder, and in later years various additions and changes in the plastic method were devised by Nélaton (1854), Thiersch (1876), Wood (1880), and others, and more recently (1917) by Kanavel, who transplanted protective fascial layers to cover the closed wall of the bladder. The great objection to the plastic closure methods is the necessity of using adjacent hair-growing skin, which later accumulates lime deposits and adds to the foulness of the uncontrolled bladder.

In 1881 Gluck and Zeller made experimental animal transplants of the ureter to the intestine; the method gave a high mortality. Trendelenburg in 1885, followed by Passavant in 1887, aided closure and bladder formation by compressing the half-formed pubic arches. König in 1896, Koch in 1897, and others, made subcutaneous section of the bony arches to aid in the development of the bladder. In 1892 Trendelenburg reported his addition to the method, that of separating the sacro-iliac joints. This method was also used by Albarran in 1909. Such procedures were of a serious nature, and a 20 per cent surgical mortality followed the formation of the uncontrolled bladder pouch, which left the patient in greater danger of subsequent renal infection.

In 1878 Thomas Smith, returning to cloacal methods, transplanted both ureters into the rectum, extraperitoneally, and in 1891 Kuester performed the same operation following removal of the bladder for cancer. In both instances the results were fatal. The first successful bilateral transplantation of the ureters after operation for cancer was that by Chalot in 1896. Chaput in 1892 had transplanted one ureter into the rectum for the cure of ureterovaginal fistula. The patient lived nine years, having three liquid stools a day. This case was reported as the first success of unilateral transplantation. The other kidney and the other ureter and the bladder were intact. Also in 1896, Maydl transplanted, intraperitoneally, the base of the inverted bladder with the attached ureters into the sigmoid; this became the popular operation. Orlow in 1904, in a study of 56 such cases, showed that 4 of 11 deaths were due to peritonitis. He reported a mortality of 17 per cent in 61 cases. Other Russian surgeons reported a mortality of 32 per cent, while Drucbert (1904) reported 27 per cent in 81 cases. Moorhead in 1916 collected 154 cases in which an early mortality of 28.5 per cent was shown. Two of three of our patients operated on by this method died. A change in the technic had been attempted by Bergenhem in 1894. He transplanted the ureters into the rectum extraperitoneally, but he was not accorded the recognition for the operation that Lendon and Peters received, who performed it in May and in July, 1899, respectively.

Jaja in 1901 performed the operation intraperitoneally, Sherman in 1905 dissected the ureters to preserve their mucous-covered small

exits, while Knaggs in 1908 operated through the Kraske incision and attached the ureters to the rectum, where they came in contact with it laterally.

Worthy of mention, from an historical standpoint, are those operations which united the early closed small bladder to the rectum, or which formed a ureterorectal fistula. This anastomosis was secured by means of a necrosis caused by tight sutures, spring forceps, or the Boari spring button. This type of operation was recommended by Lloyd and by Johnson in 1851, and by Simon in 1852.

Valve types of operation were performed by Fowler in 1898, by Martin, and by Carl Beck in 1899, and by Frank in 1901. In the 80 cases collected by Buchanan (1909) there was a 28.7 per cent mortality, practically the same as from the Maydl operation, and without the danger of peritonitis, as they were extraperitoneal.

Moynihan in 1906 changed the Maydl operation to an extraperitoneal one by uniting a very much larger inverted section of the bladder into an opening in the anterior wall of the rectum. Since 80 per cent of these cases occur in males, the operation is not difficult, and the pouch connected with the rectum is more like a true cloaca.

Rutkowski in 1898 used successfully an isolated segment of the small bowel to cover in the defective bladder.

Werelius in 1911 developed methods of partially excluding the segment of bowel to which the ureters were united by a high division of the sigmoid with side-to-side union of the proximal end with the upper rectum to re-establish the bowel continuity, and later the ureters were united separately, or by the Maydl method, to the blind end of the sigmoid.

Nature's method of emptying a duct is always by indirection, thus the salivary ducts, the common duct of the liver, and the ureters pass through the muscularis and continue for a distance between the mucous membrane and the firmer outer wall of the cavity. Pressure from within compresses the ducts and blocks against dilatation and ascending infection. Coffey has shown that the common duct is thus protected for from 2 to 3 cm. Cabot shows a similar condition in the ureterovesical entrance. Petit had called attention to this fact in 1790. The internal pressure of the contents of the bowel by gases or liquids compresses the duct in the wall according to the

tension within the intestine and yet does not interfere with the peristaltic delivery of its contents. The fact seemingly was not recognized that the mechanical principle of the passage of the ureter through the wall of the bladder and its mucosa could not be retained after the loss of its innervation. The Maydl or the Moynihan operation would be ideal could the innervation of the bladder wall be retained. In fact this was proved by Keen's case of vesicovaginal rectal fistula. The patient was cured by the closing of the vaginal entrance and was reported well with the cloacal condition twenty-two years later.

Those who believed in developing a bladder out of the remaining bladder tissue were not idle during this time. Subbotin in 1901 and Diakonow in 1908 separated a strip of the bladder wall, shaped it into a tube, and drew it through the space tunneled between the sphincter ani and the rectal mucosa; the anal sphincter closed the new urethra as well as the anus. Lerda in 1913 modified this operation by using Thiersch grafts and skin for the tube. The operative mortality in these cases was 25 per cent and the bladder still remained a septic sac; apparently the better the control the greater the danger. The next effort was to make a new bladder from a separated loop of intestine. Gersuny in 1898, and Cunéo in 1912 separated a loop of ileum, and after re-establishing the continuity of the intestine, brought one end of the loop down through a tunnel made within the anal ring, but outside of the rectal mucosa, and at a second operation transplanted, intraperitoneally, the base of the bladder into the upper end of the short segment of bowel. The Heitz-Boyer and Hovelacque operation (1912) converted the rectum into the bladder by dividing the rectosigmoid, closing the distal division, and drawing the divided sigmoid through a tunnel made by separating the anal mucosa from within its sphincter. The ureters were united with the rectum extraperitoneally or by Moynihan's method. The mobilized bowel is large; it interferes with innervation, and frequently the anal control is none too good; in fact, infants with exstrophy often have prolapse as an associated defect. This method was ingenious, but impracticable, since it was impossible to keep fecal infection from contaminating the new bladder.

Verhoogen in 1908 suggested still another method of forming a closed urinary bladder from a segment of intestine. The operation was made by dividing the ascending colon and the ileum near the

ileocecal valve; the four ends were closed and the intestinal canal completed by a side-to-side union of the ileum to the transverse colon. An appendicostomy was made by drawing the appendix through a perforation in the abdominal wall, and a catheter was passed through the appendix for irrigating the cecum. At a second operation, when the cecum was apparently clean, the base of the bladder with the ureters were united to the cecum by the Maydl method, and the cecum was emptied of urine at regular intervals by catheter. Verhoogen's first two patients died. Makkas operated successfully by this method, however, in 1910. I saw the patient two years afterward, at which time barium injection into the cecum revealed great distention of both ureters, including their terminal ends and the pelves of the kidneys, showing that the Maydl operation with the loss of innervation of the bladder wall does not afford protection to the ureters and pelves from intra-intestinal pressure. It should be taken into consideration that not only must the urine be eliminated by kidney action, but also it must be excreted from the body, instead of being placed in an absorbent area of the intestine. Berg demonstrated that when all the urine traversed the length of the colon urinary intoxication occurred. Bereznjagowski, Tichow, and Miratworzeff recommended low attachment and frequent evacuations to prevent absorption. The large bowel has few lymphatics, but it is, nevertheless, a great water absorber, especially on the right side, and filters into the veins. Because of the dangers of nephritis with the usual transplant of ureters into the intestine, it was thought by some observers that if a natural tube or duct entrance to the intestine could be utilized in uniting the ureters to the intestine, the element of sepsis would be reduced. The right ureter was therefore passed into the appendix and united there, and the left ureter was passed into the sigmoid.

Baird, Scott, and Spencer in 1917, in experimental work on dogs, seeking to avoid the dangers of infection from septic invasion of the kidney through the lymphatics of the ureter, as indicated by Sweet and Stewart, united one ureter, the right, with the larger duct of the pancreas. In this relatively clean alkalin field, apparently no lymphatic involvement occurred in from seven to ten weeks. The remaining kidney was removed and all the dogs died within twelve days from urinary intoxication. This result was anticipated by Con-

nell's experiments in 1901 in developing a bladder from closed loops of small intestine; the animals survived the first ureteral attachment and died at the second.

Every case of exstrophy of the bladder, or every case in which it is necessary to remove the bladder, must be considered, from the standpoint of operation, on its individual merits. Such considerations have to do with the age, the general condition of the patient, the functional activity of the ureters and kidneys, and in some cases, as was recommended by Edmunds and Ballance in 1886, we must be content with the deliverance of urine to the skin surface and the reliance on some collecting retention apparatus to care for the urine. The greatest dangers are apparently those of partial obstruction, causing hydronephrosis and hydro-ureter, which later may destroy the kidney by infection or cystic degeneration. Watson's method of nephrostomy has proved satisfactory. He reported three cases; one patient was living after sixteen years with tube drainage into the back. I have had one patient, a man of forty-five, in whom the bladder was removed for cancer and both ureters brought into the back, who is well after nearly ten years. The urine is collected by cup disks and carried by tubes into a urinal.

It has been recommended, under certain conditions of removal of the bladder for exstrophy with dilated ureters, to bring the ureters through lateral punctures made in the abdominal wall, and to control the urine by collectors held with an abdominal belt. Bovee collected ten such reported cases. The operation has been reported by Bottomley, Rovsing, Coffey, and others.

Harrison in 1897 performed the operation on one side and destroyed the opposite kidney by ligating its ureter. I used Sonnenberg's method of removal of the bladder in one case. After removing the bladder for cancer I attached the ureters to the proximal end of the urethra, and the urine was collected by a bulbous catheter. The patient died of nephritis during the second year after the operation. Pawlick, Summers, Chavasse, and others removed the bladder wall and developed a ureterovaginal fistula, but as approximately only 20 per cent of those afflicted with exstrophy of the bladder are females, and this procedure accomplishes only the removal of the bladder wall, it was not of general applicability.

I believe that the most satisfactory operation in cases of

exstrophy of the bladder in which the ureters are normal, or nearly so, is uniting the ureters with the rectosigmoid on the right side and to the sigmoid on the left side. There are two methods of accomplishing this, both intraperitoneal. The older method has been used by Russian and Polish surgeons, and by Stiles. These surgeons divided the ureter, isolated it from the peritoneum for some distance, and passed it into the bowel through a small puncture, where it was held by suture. The ureter was depressed into the wall of the intestine and the folds of bowel were sutured together over it for a distance of 1 inch or more; the operation is similar to that known as the Witzel method of gastrostomy or enterostomy, in which a rubber tube is used in the same manner. The operation is theoretically defective in that the channel is made of the entire thickness of the intestinal wall, and that it is too rigid to be controlled by the internal pressure. Such pressure is adequately secured by the Coffey method.

Technic of Operation for Exstrophy of the Bladder as Performed in the Mayo Clinic. A lateral abdominal 4-inch incision is made and the ureter is at once located in the pelvis behind the peritoneum. Further exposure is obtained by incising the peritoneum midway in the pelvis, over the ureter, and freeing 2 inches of the ureter. At a point about 1 inch from the bladder wall the ureter is divided between forceps, its lower end is ligated, and the peritoneum is closed by a running suture to the point at which the proximal end emerges.[1]

The anastomosis on the right side is made as low as is convenient. At a point opposite the isolated ureter an incision 1¼ inches is made through the outer coats of the bowel in the line of its longitudinal muscle (Fig. 2). The incision is carried to the mucous membrane but not through it; a slight lateral separation is made of the tissues each side of the incision, and at its lower end a puncture large enough to insert the ureter is made through the mucosa. The lower end of the ureter is split a quarter of an inch. A curved needle drawing No. 0 catgut is then passed through and

[1] Judd has modified the operative incision by making the lateral abdominal incision extend to the peritoneum, exposing and dividing the ureter extraperitoneally, opening the peritoneum at the point of its ureteral attachment, drawing out a fold of sigmoid, making the anastomosis of the ureter to it outside the peritoneum, and then replacing the bowel within the peritoneum over the incision to which it is sutured.

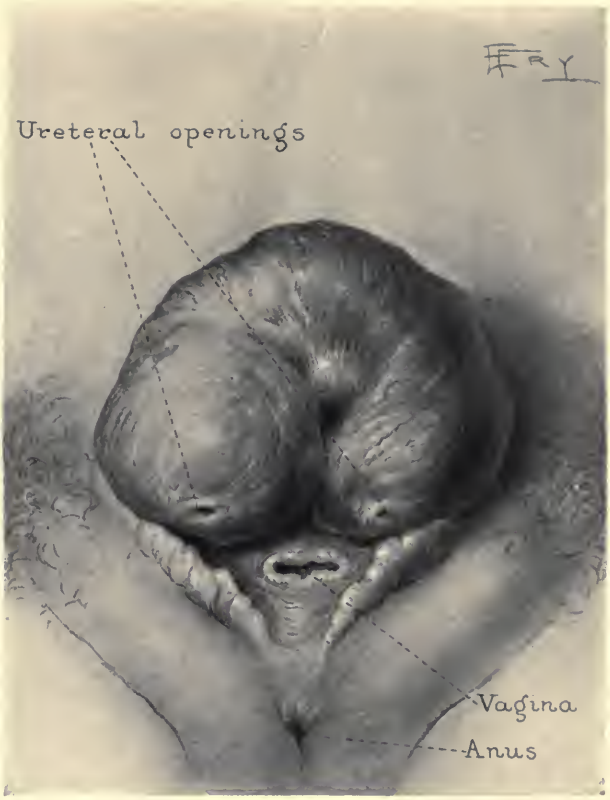

FIG. 1. CONDITION OF EXSTROPHY IN THE FEMALE.

tied to the tip of the ureter; the short end of the thread is cut away. The curved needle is passed through the opening into the intestine to emerge a half inch below the opening through the bowel (see Fig. 3). Drawing the thread draws the ureteral end within the intestine, and in order to tie and fix the ureter in position, the needle is passed through a fold of intestine at the point of emergence. Interrupted sutures approximate the divided peritoneum and muscle of the intestine over the ureter, and every other suture catches a bit of the outer wall of the ureter securely to fix its position (Fig. 4). At the upper angle of the incision an adjacent fat tag is caught by the catgut to relieve ureteral pressure. A continuous row of sutures makes additional protection over the line of the interrupted sutures; they extend over the suture which fixes the end of the ureter within the bowel (Fig. 5). Two or three additional interrupted sutures adjust the bowel to the parietal peritoneum in such a manner as to avoid kinking of the ureter and to prevent any traction on it. This method incorporates the ureter into the wall of the bowel so that the ureter, before entering the bowel lumen, is covered internally for a distance of 1¼ inches by the intestinal mucous membrane only, and any internal pressure closes the ureter; the duct entrance, similar to all duct entrances throughout the body, will close by pressure against ascending gases and liquids, but it does not prevent the

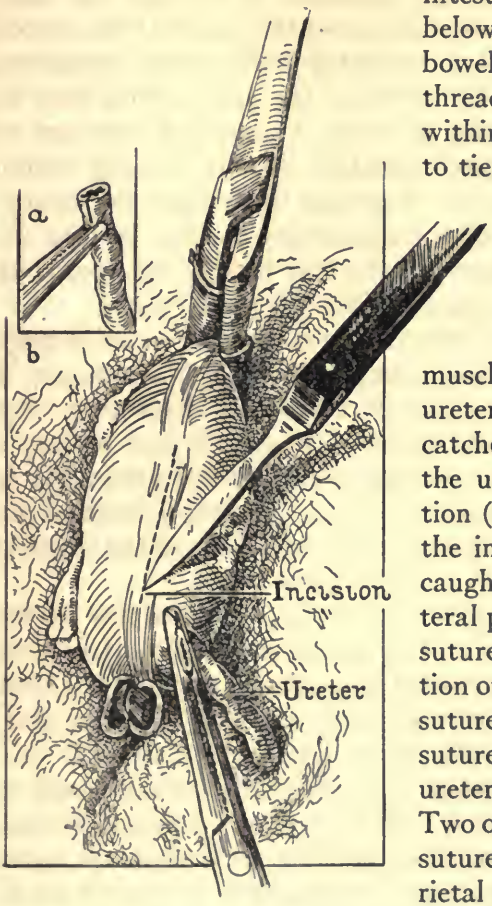

FIG. 2. *a*. Incision in End of Ureter *b*. Incision Made in Longitudinal Band of Sigmoid.

normal intermittent emptying of the ureter by peristalsis. The right side should be operated on first, as otherwise the bowel may be so shortened by a primary left operation as to make the right one difficult of accomplishment. Because of the fact that for several days after the first ureter is transplanted mild uremic symptoms develop from absorption by the bowel of the urine, which may be compared to the Murphy drip, it is best to wait for from ten to fourteen days before the second operation is done. Usually within from two to four days the urine is passing freely into the rectum. Separating the ureter for the distance necessary in order to make the anastomosis does not endanger its vitality, if it is left free from tension, as was shown by Margarucci, Monari, and Kryński.

We agree with Oppel that some degree of pyelitis occurs in most patients operated on; we believe, also, that the ultimate danger is increased by a partial obstruction of the ureter other than that afforded by pressure-control in the bowel wall. It is best to keep a perforated rubber tube in the rectum to deliver the urine; this is more important after the second operation. The third stage of the operation represents the enucleation of the bladder and the removal of the short ends of the ureters attached to it.

The most favorable age for the operation of exstrophy of the bladder is from four to ten years; it is seldom performed after thirty years. Occasionally young persons have greatly dilated ureters; after the age of thirty, dilated ureters are more common, and if double, the operation is inadvisable. We have operated on children two years of age, but we do not recommend it until they are old enough to attend to their own clothing in order to avoid constant soiling. Within a few weeks after operation children can retain the urine perfectly for from two to four hours, while adults frequently do so for from four to eight hours.

In our series of 52 patients, 6 were operated on by the plastic method; 1 died six months later (traumatic exstrophy at childbirth); 3 patients were operated on by the Maydl-Moynihan method, 2 of whom died of uremia. Twenty-six were operated on by the transplantation method, 22 successfully; 2 of these patients had but one kidney each. Four died shortly after operation. Seventeen of the 52 patients were not operated on at the time of their examination; some of them were too young and are to be operated on later;

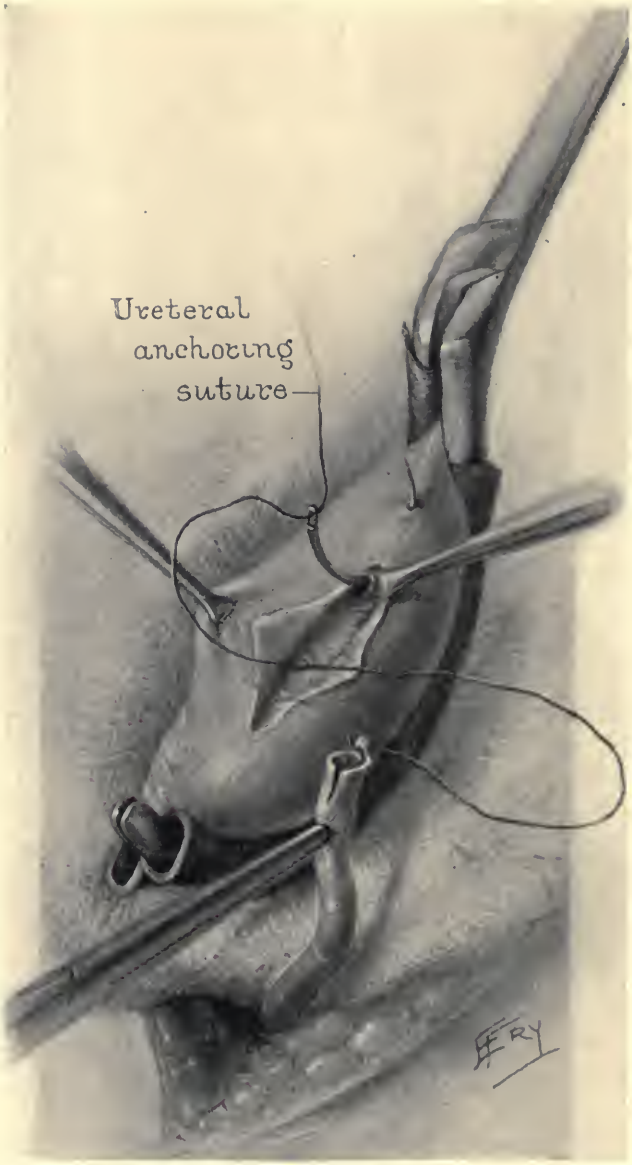

FIG. 3. MUCOUS MEMBRANE EXPOSED AND OPENING MADE IN MUCOSA TO RECEIVE URETER.

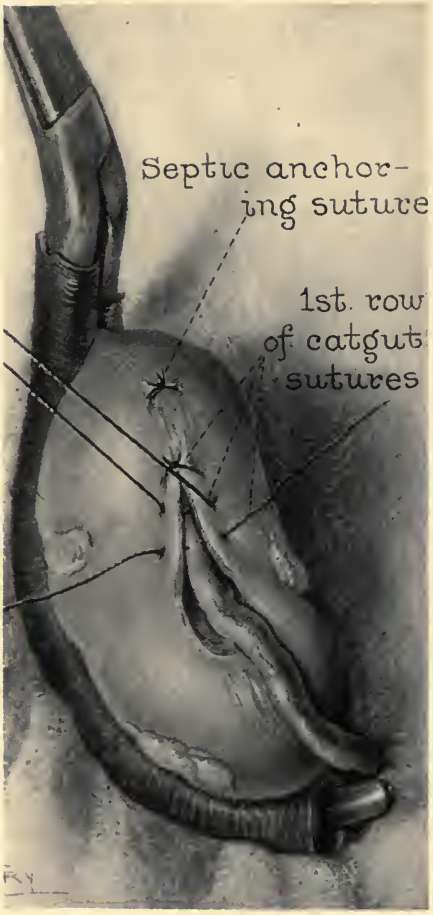

FIG. 4. CLOSURE OF PERITONEUM AND MUSCLE OVER URETER, FIXING URETER BY EVERY OTHER SUTURE.

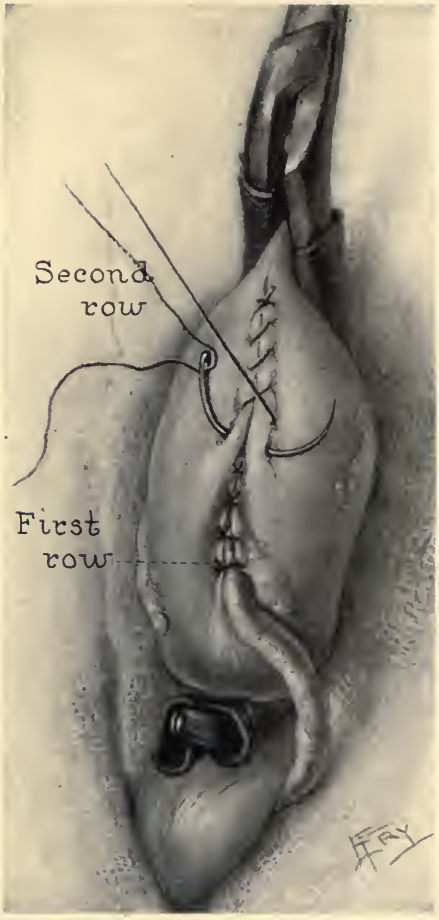

FIG. 5. ENTIRE AREA BURIED BENEATH CONTINUOUS, SEROUS. APPROXIMATING SUTURES.

others with diseased or dilated ureters were advised against the operation.

BIBLIOGRAPHY

1. Albarran, J., quoted by Zesas.
2. Baird, J. S., Scott, R. L., and Spencer, R. D., "Studies on the Transplantation of the Ureters into the Intestines," *Surg., Gynec. & Obst.*, 1917, XXIV, 482–484.
3. Beck, C., "A New Method of Operation for Exstrophy of the Bladder," *N. York M. J.*, 1900, LXXII, 311–312.
4. Bereznjagowski, quoted by Oppel.
5. Berg, J., "Om behandling af ectopia vesicæ," *Hygiea*, 1892, LIV, 62–64; *Nord. med. Ark.*, 1893; "Ueber die Behandlung der Ectopia Vesicæ," *Nord. med. Ark.*, 1907, VII, Afd., 1, n. 4, 1–22; Abstr. *J. Am. M. Ass.*, 1907, XLIX, 1409.
6. Bergenhem, B., "Ectopia vesicæ; Epispadias; lithiasis renalis; operation," *Eira*, Stockholm, 1895, XIX, 265–268; 268–273.
7. Boari, A., "Il trattamento dell' estrofia vescicale con la cisto-colostomia," *Clin. chir.*, Milano, 1900, VII; also *Atti Accad. d. sc. med. e nat. in Ferrara*, 1898–1899, LXXIII, 221; also *Policlin.*, 1895; Abstr. *Am. J. M. Sc.*, 1896, CXI, 481.
8. Bottomley, J. T., "Operative Treatment of Exstrophy of the Bladder by Transplantation of Ureters on to the Skin of the Loin: Application of the Principle to other Bladder Surgery—Report of Two Illustrative Cases," *J. Am. M. Ass.*, 1907, XLIX, 141–144.
9. Bovee, J. W., "A Critical Survey of Ureteral Implantations," *Ann. Surg.*, 1900, XXXII, 165–193.
10. Buchanan, J. J., "Remote Results of Implantation of the Ureters into the Bowel for Exstrophy. A Consideration of the Extraperitoneal Method of Bergenhem," *Surg., Gynec. & Obst.*, 1909, VIII, 146–155.
11. Cabot, H., "Modern Urology," Philadelphia, Lea & Febiger, 1918, II, 32–65.
12. Chalot, quoted by Peterson.
13. Chaput, "L'abouchement des uretères dans l'intestin," *Archiv. gén. de méd.*, 1894, CLXXIII, 5–31.
14. Chavasse, "A Case Illustrating a Method of Treating Extroversion of the Bladder in the Female," *Lancet*, 1899, I, 161–162.
15. Coffey, R. C., "Physiologic Implantation of the Severed Ureter or Common Bile-Duct into the Intestine," *J. Am. M. Ass.*, 1911, LVI, 397–403.

16. Connell, F. G., "Exstrophy of the Bladder," *J. Am. M. Ass.*, 1901, XXXVI, 637–668.
17. Cunéo, Heitz-Boyer, and Havelacque, "Exstrophie de la vessie. Création d'une vessie nouvelle. Obsérvations et procédés opératoires," *Bull. et mém. Soc. de chir.*, 1912, XXXVIII, 2–24.
18. Diakonow, O. P. J., "A Contribution to the Question of Exstrophy of the Urinary Bladder," *Surg., Gynec. & Obst.*, 1908, VII, 695–700.
19. Drucbert, J., "Les résultats éloignés de l'opération de Maydl dans l'exstrophie vésicale," *Écho méd. du nord.*, 1904, VIII, 481–484.
20. Duncan, A., "An Attempt towards a Systematic Account of the Appearances Connected with that Malconformation of the Urinary Organs, in which the Ureters, instead of Terminating in a Perfect Bladder, open Externally on the Surface of the Abdomen," *Edinb. M. & Surg. J.* 1805, I, 43; 132.
21. Edmunds, W., and Ballance, C. A., "Diverting the Ureters and Removing the Bladder," *St. Thomas's Hosp. Rep.*, 1886, XVI, 201–207.
22. Fowler, G. R., "Implantation of the Ureters into the Rectum in Exstrophy of the Bladder, with a Description of a New Method of Operation," *Am. J. M. Sc.*, 1898, CXV, 270–276.
23. Frank, J., "Ureteral Implantation into the Bowel for Diversion of the Urine," *J. Am. M. Ass.*, 1901, XXXVI, 1466–1469; "Vesicorectal Anastomosis with Special Reference to the Treatment of Exstrophy of the Bladder," *J. Am. M. Ass.*, 1900, XXXIV, 1174–1178; 1237–1241.
24. Gersuny, R., *Wien. klin. Wcbnscbr.*, 1898, No. 43, quoted by Connell.
25. Gluck, T. and Zeller, A., "Ueber Exstirpation der Harnblase und Prostata," *Arch. f. klin. Chir.*, 1881, XXVI, 916–24.
26. Harrison, R., "Extroversion of the Bladder," *Lancet*, 1897, I, 1091.
27. Heitz-Boyer, M., and Hovelacque, A., "Création d'une nouvelle vessie et d'un nouvel urètre," *Jour. d'urol. méd. et chir.*, 1912, I, 237–258.
28. Holmes, F., "On Congenital Extroversion or Exstrophy of the Bladder; and on a Method of Alleviating Some of its Effects by a Plastic Operation," *Lancet*, 1863, I, 714–715.
29. Jaja, F., "Contributo allo studio della sutura immediata dell' uretra nelle rotture traumatiche," Morgagni, 1902, I, 373–383; also *Atti d. Soc. ital. d. chir.*, Roma, 1901.
30. Johnson, A., quoted by Holmes.
31. Judd, E. S., personal communication to author.
32. Kanavel, A. B., "Transplantation of Fascia Lata in Exstrophy of the

Bladder, Complete Defects in the Abdominal Wall, and Spina Bifida," *Surg. Clin.*, Chicago, 1917, I, 153–167.

33. Keen, W. W., "The Surgical Complications and Sequels of Typhoid Fever," Philadelphia, Saunders, 1898, 80–82.
34. Knaggs, R. L., "A Case of Implantation of the Ureters into the Rectum for Exstroversion of the Bladder in a Woman, by a Modified Peters' Operation," *Brit. M. J.*, 1908, II, 1233–1234.
35. Koch, C. F. A., "Eine modificirte Trendelenburg'sche Blasenspaltenoperation," *Centralbl. f. Chir.*, 1897, XXIV, 953–956.
36. König, *Verhandl. d. deutsch. Gesellsch. f. Chir.*, 1896, I, 77.
37. Kryaski, L., "Zur Technik der Ureterenimplantation in den Mastdarm," *Centralbl. f. Chir.*, 1896, XXIII, 73–75.
38. Küster, E., "Neue Operationen an Prostata und Blase," *Arch. f. klin. Chir.*, 1891, XLII, 858–878.
39. Lendon, A. A., "Extroversion of the Bladder," *Brit. M. J.*, 1906, I, 961–964.
40. Lerda, G., "Contribution au traitement de l'exstrophie de la vessie," *Jour. de chir.*, 1913, X, 549–562.
41. Lloyd, "Ectrophia Vesicæ (absence of the anterior walls of the bladder); Operation; Subsequent Death," *Lancet*, 1851, II, 370–372.
42. Lower, W. E., "Malformations and Diverticulum of the Bladder," Cabot, H., ed. *Mod. Urol.*, Philadelphia, Lea & Febiger, 1918, II, 32–65.
43. Makkas, M., "Zur Behandlung der Blasenektopie. Umwandlung des ausgeschalteten Coecum zur Blase und der Appendix zur Urethra," *Centralbl. f. Chir.*, 1910, XXXVII, 1073–1076.
44. Malone, B., "A Discussion of the Different Methods of Exclusion in the Treatment of Exstrophy of the Bladder, with Case Report," *Tr. South. Surg. Ass.*, 1916, XXIX, 240–246.
45. Margarucci, O., "Ricerche sulla circolazione propria dell' uretere," *Policlin.*, 1893–94, I, 321–324; also *Atti. d. XI Cong. med. internaz.*, 1894, Roma, 1895, IV, 563–5.
46. Martin, F. H., "Implantation of Ureters in Rectum, "*J. Am. M. Ass.*, 1899, XXXII, 159–161.
47. Maydl, K., "Ueber die Radikaltherapie der Ectopia vesicæ urinariæ," *Wien. med. Wchnschr.*, 1894, XLIV, 1113; 1169; 1256; 1293; "Neue Beobachten von Ureteren-implantation in die Flexura romana bei Ectopia vesicæ,"1896, XLVI, 1241; 1333; 1374.
48. Mayo, C. H., "Exstrophy of the Bladder and its Treatment," *J. Am. M. Ass.*, 1917, LXIX, 2079–2081.
49. Mirotworzeff, S. R., quoted by Oppel.

50. Monari, U., "Ueber Ureter-Anastomosen; experimentelle Untersuchungen," *Beitr. z. klin. Chir.*, 1895–96, XV, 720–734, quoted by Connell.
51. Moorhead, J. J. and E. L., "Exstrophy of the Bladder," *J. Am. M. Ass.*, 1916, LXVI, 409–411.
52. Moynihan, B. G. A., "Extroversion of the Bladder. Relief by Transplantation of the Bladder into the Rectum," *Ann. Surg.*, 1906, XLIII, 237–240.
53. Nélaton, *Gaz. hebd. de méd.*, 1854, I, quoted by Connell.
54. Neudörfer, J., "Die Operation der Ectopie der Blase," *Fortschr. d. Med.*, 1886, IV, 255–258; quoted by Boogher, L., "Exstrophy of the Bladder," *Urol. & Cutan. Rev.*, 1916, XX, 376–377.
55. Oppel, W. A., "Exclusion of the Bladder, *Urol. & Cutan. Rev.*, Tech. Suppl., 1913, I, 1–22.
56. Orlow, L., "Traitement opératoire de l'exstrophie de la vessie; transplantation des uretères par le procédé de Maydl," *Rev. de gynéc. et de chir. abd.*, 1903, VII, 795–852.
57. Passavant, G., "Die Blasen-Harnröhrennaht mit Vereinigung der Schambeinspalte bei angeborener Blasenspalte und Epispadie," *Arch. f. klin. Chir.*, 1887, XXXIV, 463–500; 1890, XL, 1–61.
58. Pawlick, "Ueber Blasenexstirpation," *Wien. med. Wchnschr.*, 1891, XLI, 1814–1816.
59. Peters, G. A., "Transplantation of Ureters into Rectum by an Extraperitoneal Method for Exstrophy of Bladder," *Brit. M. J.*, 1901, I, 1538–1542.
60. Peterson, R., "Anastomosis of the Ureters with the Intestine," *J. Am. M. Ass.*, 1901, XXXVI, 569–573.
61. Petit, *Trait. des mal. chir.*, 1790, III, 4, quoted by Connell.
62. Roux, J., "Exstrophie de la vessie; autoplastie; insuccès; établissement définitif d'un canalcutané propre à maintenir en place un reservoir en caoutchouc vulcanisé," *Union méd.*, 1853, VII, 449–453.
63. Rovsing, T., "Totalexstirpation der Harnblase mit doppelseitiger lumbaler Ureterostomie," *Arch. f. klin. Chir.*, 1907, LXXXII, 1047–1054.
64. Rutkowski, M., "Zur Methode der Harnblasenplastik," *Centralbl. f. Chir.*, 1899, No. 16; Editorial in *Ann. Surg.*, 1899, XXX, 238–243.
65. Sherman, H. M., "Exstrophy of the Bladder Successfully Treated by Peters' Method. *J. Am. M. Ass.*, 1905, XLV, 890–891.
66. Simon, J., "Ectropia vesicæ; Operation for Directing the Orifices of the Ureters into the Rectum; Temporary Success; subsequent death; Autopsy," *Lancet*, 1852, II, 568–570; "Congenital Imperfection of

the Urinary Organs Treated by Operation," *Tr. Path. Soc. Lond.*, 1855, VI, 256–258.

67. Smith, T., "An Unsuccessful Attempt to Treat Extroversion of the Bladder by a New Operation," *St. Barth. Hosp. Rep.*, 1879, XV, 29–35.
68. Sonnenberg, "Die Endresultate operativer Verfahren bei Ektopia vesicæ," *Deutsch. med. Wchnschr.*, 1899, XXV, 219–220.
69. Spooner, H. G., Report of a Case of Exstrophy of the Bladder, with a Consideration of Operative Treatment," *Boston M. & S. J.* 1905, CLII, 546–548.
70. Stiles, H. J., "A Boy with Extroversion of the Bladder, in whom the Ureters had been Transplanted into the Rectum after the Method of Peters, of Toronto," *Tr. Med.-Chir. Soc. Edinb.*, 1902–03, n.s., XXII, 133–135; "Epispadias in the Female and its Surgical Treatment," *Surg., Gynec. & Obst.*, 1911, XIII, 127–140.
71. Subbotin, M., "Neues Verfahren zur Bildung der Harnblase und Harnröhre mit einem Sphinkter aus dem Mastdarm bei Exstrophia Vesicæ, Epispadie hohen Grades und Urininkontinenz," *Centralbl. f. Chir.*, 1901, XXVIII, 1257–1260.
72. Summers, quoted by Bottomley.
73. Sweet, J. E., and Stewart, L. F., "The Ascending Infection of the Kidneys," *Surg., Gynec. & Obst.*, 1914, XVIII, 460–469.
74. Thiersch, C., *Verhandl. d. deutsch. Gesellsch. f. Chir.*, 1882, XI, 89; also *Centralbl. f. Chir.*, 1876, 504, quoted by Connell; "Zwei Fälle von operativ geheilter Inversio vesicæ," *Berl. klin. Wchnschr.*, 1892, XIX, 471.
75. Tichow, quoted by Oppel.
76. Trendelenburg, F., "Zur Operation der Ectopia vesicæ," *Centralbl. f. Chir.*, 1885, XII, 857–860; "Ueber Operationen zur Heilung der angeborenen Harnblasen- und Harnröhrenspalte," *Arch. f. klin. Chir.*, 1892, XLIII, Festschr., 394–438.
77. Verhoogen, J., "Neostomie urétéro-cæcale; formation d'une nouvelle poche vésicale et d'un nouvel urètre." *Ass. franç. d'urol. Proc.-verb.*, 1908, Paris, 1909, XII, 362–365.
78. Watson, F. S., "The Operative Treatment of Tumors of the Bladder," *Ann. Surg.*, 1905, XLII, 805–830.
79. Werelius, A., "Operative Method for Exstrophy of Bladder; with Report of a Case," *Surg., Gynec. & Obst.*, 1911, XII, 158–159.
80. Winslow, R., "Report of a Case of Exstrophy of the Bladder Operated on Nearly Thirty Years Ago, with Subsequent History," *Surg., Gynec. & Obst.*, 1916, XXII, 350–352.

81. Witzel, O., "Zur Technik der Magenfistelanlegung," *Centralbl. f. Chir.*, 1891, XVIII, 601–604; "Die Sicherung der Gastroenterostomose durch Hinzufügung einer Gastrostomose (Gastroenterostomosis externa)," *Centralbl. f. Chir.*, 1899, XXVI, 1193.
82 Witzel, O., and Hoffman, C., "Die Gastroenterostomosis, Gastrostomosis und ihre Verbindung zur Gastroenterostomosis externa," *Deutsch. med. Wchnschr.*, 1900, XXVI, 301–303; 325–327; 342–346.
83. Wood, J., "Exstrophy of the Bladder," *Brit. M. J.*, 1880, I, 278.
84. Zesas, D. G., "Die Implantation der Ureteren in den Darm," *Deutsch. Ztschr. f. Chir.*, 1909, CI, 233–266.

SOME NOTES ON ACHYLIA GASTRICA

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In discussing achylia gastrica, or, to be more exact, achlorhydria met with in other conditions than pernicious anemia, it is well to note at first the steady increase in the number of conditions, functional as well as organic, in which absence of free hydrochloric acid is met with in a greater or less proportion of cases.

Let us simply enumerate some of these; some obviously to be regarded as of primary or essential, others of definitely secondary type, and in these various pathological entities we find representatives of all the theoretically possible causes from the pathological-physiological standpoint; psychogenic, neurogenic, reflex, toxic, inflammatory, infectious, due to disturbance in blood supply, to errors of metabolism, to disturbance of the normal secretory stimuli of nervous, or of hormonic origin. In the post-mortem study of these cases we therefore find, as we would expect, very marked, or very slight, or no pathological changes in the glands devoted to secretion of acid and pepsin, while *pari passu* with this we find, clinically, that in certain cases a complete return of normal secretion is possible, in other cases a partial return, while in still others the lack of acid and pepsin is a permanent condition.

Let us run over, seriatim, the most important pathological conditions in which complete absence of free and combined hydrochloric acid, and, according to our experiments, as a rule, marked diminution or absence of pepsin is met with.

1. The last stages of chronic gastritis—alcoholic, due to dietetic errors, or due to teeth, tonsillar, nasal, pharyngeal infections, etc.

2. Gout and arthritis deformans, or, perhaps, better called chronic infectious arthritis, leading in the first case to the substitution of an acid for an alkaline therapy, and in the latter to the belief held by many in the intestinal origin of the disease.

3. Various infectious diseases—tuberculosis, where it is often found, and typhoid fever, in the latter of which in a number of cases

we have found a complete achylia following the disease, which may be one of the causes of the gastrointestinal symptoms often met with, which is probably toxic in origin and not due to destructive changes in the glands, as in many cases, after a considerable period of time—in several of our cases more than a year—there was a gradual return to normal gastric juice, and in all these cases the use of hydrochloric acid therapy should be advised; syphilis, sinusitis, pyorrhea alveolaris—a very frequent cause, probably leading to a true infectious gastritis, and being the most potent factor in the gastric dyspepsia and diarrhea in older people—and tonsillitis.

4. Various intestinal parasitic diseases, especially infection with the uncinaria—hookworm disease, though frequently found in infections with tapeworm, round worm, and entamœba, peculiarly interesting as an expression of a toxic achylia of intestinal origin, and thus of especial interest in connection with pernicious anemia. Incidentally, a blood picture very similar to that of pernicious anemia may be produced by repeated injections of the juice expressed from certain of these parasites.

5. Conditions associated with chronic passive congestion, notably chronic nephritis and myocardial disease.

6. Pellagra and sprue—in the latter associated frequently with a concomitant absence of pancreatic secretion, and in each disease a marked improvement of the digestive symptoms often following the administration of hydrochloric acid, in association with pancreatic ferment in the case of sprue, with, in the latter, a return to normal gastric contents and the marked improvement of general symptoms met with in quite a number of these cases.

7. Cancer, not only of the stomach, but often of other organs, even outside the abdominal cavity, especially in the late stages of the disease.

8. Diseases of the thyroid; and here, both in Graves's disease, or hyperthyreosis, and myxedema, or hypothyreosis, it is often found, and is probably the cause of the marked diarrhea which may be the only symptom of the former disease.

9. Linitis plastica, or cirrhosis of the stomach, probably representing, in most cases, the conversion of an old ulcer into a malignant condition, with marked hyperplasia of the fibrous tissue and very little cellular participation.

10. High grades of ptosis and atony of the stomach, although here hyperacidity or normal acidity may also be found.

11. Chronic gall-bladder disease with and without jaundice, where we have found it in a very considerable proportion of cases, and where it may prove of real aid in diagnosis.

12. After sudden shock, violent emotions, worry, and overwork, also frequently during the menstrual period.

Truly a large group of cases, and very interesting, as it makes one realize under what various stimuli—infectious, toxic, nervous, etc.—the condition may develop, and how difficult it may be to differentiate the true underlying condition. Unlike many others, we have not found the presence of pepsin in large amount of much value in differentiating the purely functional from the organic achlorhydrias, for in a large series in which the pepsin was estimated quantitatively by the edestin method we found in the great majority of cases, both functional and organic, the practical disappearance of pepsin *pari passu* with that of the hydrochloric acid. The effect of the absence of hydrochloric acid is very varied, and in many cases difficult to explain, as, for example, the fact that in certain cases it is associated with a diarrhea, in others with constipation, and in still others with a normal bowel habit. After all, to appreciate what the absence of hydrochloric acid may bring about we must always keep in mind its multiplex functions—its action upon the pyloric sphincter; its rôle in converting the inactive prosecretin into the active hormone of the pancreas, secretin; its disinfecting properties; its rôle in the digestion of the proteins; the essential part it plays with pepsin in the digestion of connective tissue, and its activating power upon the zymogens of pepsin and rennin.

There are certain peculiarly interesting problems which arise in connection with the study of this subject, as, for example, the rather striking increase in the soluble proteid contents of the gastric contents in the achylia met with in carcinoma, of real value in differential diagnosis; our demonstration by stool studies that in practically all the achylias except those met with in sprue, the pancreatic ferments are practically normal in quality. This is interesting, in the first place, in calling attention to the fact that we must assume a nervous, as well as a hormonic mechanism in the elaboration

of the pancreatic secretions—at least, in pathological conditions—thus supporting Pawlow's views (and opposing those of Starling), that hormonic stimulation cannot explain the whole phenomenon of secretion in the gastrointestinal tract below the gastric level, and, in the second place, definitely opposing Gross's view that in gastrogenous diarrheas met with in achylia there is a concomitant diminution of pancreatic ferments.

Another point of great interest, and one which has not yet been satisfactorily explained, is why certain achylias are associated with diarrhea, others with normal motor function of the bowels, others with hypomotility; certainly not to be explained in our experience on the theory that in the herbivor type the achylias are likely to be associated with diarrhea, in the carnivor type with constipation; and in the second place, the minimum amount of hydrochloric acid which is necessary—not more than a few per cent of the normal amount secreted with an ordinary meal, which can absolutely control the diarrhea in the majority of these cases. Another point of peculiar interest is the extreme hypersensitiveness to acid medication met with in certain of these cases of achylia gastrica—a few drops of any acid, even lactic or citric acid, producing marked discomfort, even great pain; and in the last place the frequency with which, if gastric symptoms are present, they simulate symptoms of hyperchlorhydria, which is probably best explained by the associated vagal hyperesthesia met with in both cases; and last of all, in the great majority of these cases of achylia the gastric symptoms are very slight or *nil*, the symptoms dominating the picture being almost entirely intestinal.

EPIDEMIC PNEUMONIA

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THE history of medicine records many epidemics of pneumonia, sometimes in association with other diseases, sometimes spreading independently. No very precise idea of the nature of these epidemics or of the reasons for their epidemic character can be derived from these records, because nearly all occurred before the era of bacteriological studies, but the epidemics of the year 1918 should furnish much material for the solution of these problems, since they have been very diligently studied.

It appears that there were in the United States two great epidemic outbreaks of pneumonia, the first closely associated with measles, lasting through the winter and spring, the second immediately following the sudden sweep of influenza across the continent in the late summer and autumn. In the interval there were small epidemics here and there, but nothing that attracted general attention. It is true that during the season in which lobar pneumonia ordinarily occurs there were scattered cases of this disease in about the usual proportion.

The First Epidemic. In the winter and spring measles was extremely prevalent among the men of the drafted troops who came from remote rural districts. It had the ordinary characters, but cultures and smears showed that many of these men harbored in their throats a hemolytic streptococcus. This readily spread in crowded wards to the throats of others. It was thought and afterward proven that if the clean measles patients could be kept separate from those with infected throats most of the pneumonia might be avoided.

The deaths in this pneumonia followed a brief but severe illness, the outstanding features of which were extreme inspiratory dyspnea with a livid cyanosis, and in most cases the signs of extensive pleural effusion. There was usually a definite leucocytosis. At

autopsy the lungs presented a great variety of conditions, but the study of a long series of cases appears to permit one to consider these under two main headings, although combinations of these must be recognized. In each of these groups several stages are distinguishable, and the presence of an abundant pleural effusion may introduce modifications of another kind. It seems permissible to anticipate what must be written of the details of these conditions and to present the view that in the first of these groups we have the effect of bacteria invading the tissues of a resistant host, while in the second the host displays very slight resistance. The frequent combination of the lesions characteristic of these groups would suggest that the lowering of resistance may be due to the production of an allergic or hypersensitive state.

In practically all of these cases a hemolytic streptococcus was the predominant organism, and this was distributed in such relation to the lesions that there could be no doubt of its significance as the essential cause of the pneumonia. In some cases the influenza bacillus of Pfeiffer was also present, and in two or three it was the predominant organism in the lung, so that those rather peculiar cases were regarded as illustrating the lesions produced by that bacillus. The pneumococcus was present in some cases in areas of typical lobar pneumonia, while the rest of the lung was occupied by characteristic streptococcal pneumonia.

Interstitial Broncho-pneumonia. This name has been given to the combination of bronchitis and nodular consolidation produced by the streptococcus in the lungs of a resistant person. It is primarily a purulent bronchitis with a zone of hemorrhage about each bronchiole, and intense infiltration of the bronchial wall with leucocytes and mononuclear cells. The streptococci remain almost entirely restricted to the purulent exudate in the bronchi, and although they are found in numbers in the lymphatics of the lung, through which they extend to infect the pleura, they are not found in the alveolar exudate.

In the more advanced stages the bronchi are still found to contain a purulent exudate, but their walls are enormously thickened by the great vascularization, new formation of granulation tissue, and especially by an extraordinary accumulation of mononuclear wandering cells in the interstices of the tissue. The epithelium is

merged into a necrotic false membrane or has disappeared. Streptococci lie in great numbers along the lining surface of the bronchiole. The neighboring alveoli are filled with dense plugs of fibrin together with desquamated epithelial cells, lymphoid cells, and red corpuscles. The alveolar walls are greatly thickened by an infiltration of the same mononuclear cells and by new formation of connective tissue. This fades away in alveoli more distant from the bronchiole, but reappears to some extent in the neighborhood of the interlobular septa. The alveolar exudate also changes in character as one passes away from the bronchi and the dense plugs of fibrin, which are often partly replaced by vascular connective tissue, disappear, and give place to blood and finally to a viscid fluid.

The interlobular septa are greatly thickened by edema, infiltration with mononuclear wandering cells, and the new formation of connective tissue, and are rendered especially conspicuous by the great distention of the accompanying lymphatics with a purulent clot rich in bacteria. There can be no stream of lymph in such an occluded channel, and the streptococci must reach the pleura by actual growth rather than by any passive transportation. The pleura is thickened by a newly formed granulation tissue and is covered with a fibrinopurulent exudate.

The gross appearance of the lung corresponds with these progressive changes. In the beginning the surface is smooth, there is no fluid in the pleural cavity, and the lung is distended with air. On the cut surface the bronchi and bronchioles can be traced by their thickened gray walls, their content of grayish-yellow pus, and the halo of hemorrhage which surrounds them. In later stages the pleural cavity contains a quantity of thin, greenish-brown fluid with a granular sediment and shreds of fibrin. The pleural surface is covered with shaggy fibrin unevenly distributed and the pleura itself is thickened. The lung is collapsed, partly as a result of the obstruction of the bronchi, partly from the pressure of the pleural effusion. Throughout its substance there can be felt firm nodules or more extensive masses of consolidated tissue. Upon the cut surface the lobules are marked out very distinctly by the conspicuously thickened interlobular septa, which sometimes appear as prominent white, beaded bands. In the lobules there are usually several firm nodules clustered about the terminal branches of the bronchiole,

each showing in its center the lumen of a bronchiole filled with pus. If these bronchioles happen to be cut longitudinally, it is seen that their walls are greatly thickened and that the firm nodule forms a mantle about them for a short distance. This is surrounded by a zone of hemorrhage and edema. In still older cases such peribronchial areas extend so as to become confluent and form quite large patches of consolidation, which are sometimes pale yellow with a background of hemorrhage. Retrogression may occur if the patient survives longer and the pleural exudate assumes a purulent character, and unless evacuated is encapsulated by dense adhesions.

Lobular Pneumonia. The other type of pneumonia caused by invasion of the hemolytic streptococcus in the lung of a less resistant person presents none of the barricading process just described and none of the restriction of the growth and spread of the streptococci. The name lobular pneumonia is arbitrarily given, although perhaps not entirely suitable, to distinguish it from the interstitial broncho-pneumonia. In these cases, which run a rapid course, there is no marked reaction in the framework of the lung. The streptococci are present in enormous numbers in the purulent and hemorrhagic bronchial exudate and in equally great numbers in the bloody purulent exudate in the alveoli throughout considerable areas. They grow into a perfect feltwork of chains, as though in the best possible culture medium. The bronchial and alveolar walls are not infiltrated with wandering cells, but together with the contained exudate become necrotic throughout large areas.

The gross appearance of the lung corresponds precisely with this. There is usually a bloody pleural exudate; the pleural surface is hemorrhagic and roughened by fibrin. The partly collapsed lung contains confluent areas in which the consolidated tissue is deep red or almost black as a result of the abundant hemorrhage, but there are areas of gray opaque tissue where necrosis is most advanced. There are no nodular consolidations about the bronchi, and interlobular septa and bronchial walls are inconspicuous, although the lymphatics may be distended with purulent and bloody exudate.

It is by no means uncommon to find small patches of intra-alveolar purulent and hemorrhagic exudate, with abundant streptococci, scattered in the tissue in cases in which the predominant changes are those of the interstitial broncho-pneumonia. It seems that this may

be explained as the result of hypersensitization of the tissue produced by the original resisted infection.

The Second Epidemic. The epidemic disease, influenza, as all know, swept with great rapidity over the whole country from east to west. Its nature is still entirely obscure, in spite of the diligent studies made in every camp laboratory and hospital. The view which at first seemed most plausible, that it was due to the influenza bacillus of Pfeiffer, has not been substantiated by any proof, although this organism has been found in the throats and even in the lungs in a great number, perhaps in the majority of cases. It is, however, known to be a common inhabitant of the throats of normal persons, and might be expected to occur with increased prevalence among people whose resistance was lowered by such a disease as epidemic influenza, just as the pneumococcus and other organisms were more frequently found in significant numbers in these throats.

In some districts the influenza bacillus was found in practically every case—in others only rarely. There has been much difficulty with the cultivation of this organism, since it requires special media for its growth. Even the media which contain hemoglobin are vitiated, as Rivers shows, by the presence of inhibitory substances in certain sera. This may explain the lack of success experienced by some investigators in its cultivation, but it scarcely justifies the more successful in other parts of the country in their claim that influenza bacilli are really equally prevalent everywhere.

The epidemic influenza has many of the characters of an acute exanthematic disease such as measles. Bloomfield has observed a rash in many cases and a characteristic enanthem, and has also found that, as in measles, the von Pirquet reaction fails during the height of the disease, only to appear when the fever is over. It is accompanied by a marked leukopenia and other evidences of an extreme lowering of resistance to bacterial invasion.

The pneumonia which followed the influenza was extraordinarily fatal, and was characterized especially by its rapid course and by the abundance of the bacteria found in the exudate. The anatomical type of the pneumonia itself was determined by the character of the invading organism, and while there were often mixed infections, there was, as a rule, one predominating organism which established the type. In our own experience the influenza bacillus was by no

means always present. Cultures, animal inoculations, smears, and especially accurate staining of the sections of the lungs showed this. On the other hand, when it was present in predominant numbers it produced a perfectly characteristic type of pneumonia. At Camp Lee in Virginia and at the Johns Hopkins Hospital in Baltimore it was rarely found, while at Camp Dix in New Jersey it was present in every case.

The organisms concerned were the several types of pneumococcus, the staphylococcus aureus, the hemolytic streptococcus, and the influenza bacillus.

The pneumonia caused by the pneumococcus was a confluent lobular pneumonia which in late stages assumed the form of lobar pneumonia. In the most acute cases there was no pleural exudate; the pleural surfaces showed blotches of opaque bloody discoloration like red paint. There were indefinite or sharply lobular patches of consolidation. On section these areas were red, smooth, elastic, fairly firm, and elevated above the surrounding tissue. They were extremely moist and exuded a viscid bloody fluid. A gelatinous red fluid could be seen in the terminal bronchioles and ductuli alveolares—no plugs of opaque exudate projected from the alveoli. The bronchi were slightly reddened or pale, and contained only a frothy fluid. Later stages showed patches in the center of such elastic areas, in which the alveoli were filled with opaque fibrinous plugs, and finally this appearance spread to the whole area and to adjacent confluent areas of consolidation.

Microscopically the early stages showed an extremely fresh, delicate exudate of fibrin with red corpuscles, leucocytes, and mononuclear cells in the alveoli. The ductuli alveolares were distended with fluid and lined with a rather thick layer of hyaline material, which overlay the epithelium and failed to give the reactions for fibrin. Pneumococci were present in the exudate in enormous numbers.

The pneumonia caused by the hemolytic streptococcus was precisely like that described as lobular pneumonia in the first epidemic, although it seemed that the streptococci were, if possible, more abundant than before, and had caused more widespread necrosis and hemorrhage. There was great edema, the bronchi being filled with frothy fluid. No trace of the interstitial infiltration and indura-

tion so commonly seen in the form which followed measles was to be observed in these cases. It is to be noted that recent reports which describe pneumonia occurring months after the epidemic of influenza had passed over, state that the proportion of cases due to the hemolytic streptococcus is very greatly increased. It is suggested that as a result of frequent passage through human beings this streptococcus has acquired a great virulence, which permits it to invade the lungs of normal persons without the assistance of a predisposing disease.

The pneumonia following infection with the staphylococcus aureus was not well represented in our series, since we had only a few cases in which there was a mixed infection, but Dr. Chickering, who observed many cases, describes it as a specific form in which, upon the basis of a rather diffuse inflammatory process, minute abscesses ultimately develop throughout the lung. In these the organisms are present in great numbers.

The pneumonia caused by the influenza bacillus of Pfeiffer seems to have been common in the New England States. We encountered a number of cases in the epidemic at Camp Dix in which the influenza bacillus was the predominant organism and sometimes present in pure culture. In these there was a pneumonic lesion entirely different from those caused by the pneumococcus or streptococcus. It resembled, rather, the interstitial broncho-pneumonia, and may be most accurately described by that name. The bacilli often in large numbers were restricted to the bronchi. None were found in the lymphatics, which were collapsed and inconspicuous, nor were any found in the pleural cavity, since in most cases this was obliterated by adhesions.

The bronchial exudate was composed of polymorphonuclear leucocytes, many of which were active phagocytes. The bronchial walls were enormously thickened, not only by infiltration with leucocytes and lymphoid and plasma cells, but also by an extensive new growth of connective tissue cells. The adjacent alveoli contained dense plugs of fibrin with desquamated epithelial cells and many leucocytes. There was no great admixture of red blood corpuscles, but widespread organization of the exudate had occurred. The exudate differed from that seen in the streptococcal interstitial broncho-pneumonia in the greater proportion of leucocytes found there. No influenza bacilli were found in this alveolar exudate. The

alveolar walls were greatly thickened by a process identical with that in the bronchial walls.

The gross appearance of such a lung was entirely different from that of the lung in which pneumonia was caused by the pneumococcus. These lungs were rather pale and dry, the bronchi filled with thick, yellow, sticky, purulent exudate. The pleural surface was smooth or roughened by adhesions. Most of the lung substance was air-containing, but studded throughout with firm, shot-like nodules and some larger solid masses. Upon incision these were found in relation to the bronchioles as prominent yellow nodules, the cut surface of which was dense, smooth, and shining, sometimes rather gray and translucent, and showing in the center the lumen of a bronchiole filled with pus. The larger areas were obviously due to the confluence of such nodules.

This condition is, therefore, in every respect comparable with the interstitial broncho-pneumonia caused by the streptococcus, although it seems to indicate that since such resistance and barricade formation can be evidenced in a person recently affected by the influenza, the virulence of the influenza bacillus must be less than that of the streptococcus. It emphasizes this analogy to find that in certain cases there are, in addition to the nodules of interstitial infiltration with organized exudate, patches of alveoli which are thin-walled, but filled with an exudate of leucocytes with myriads of influenza bacilli. This is quite comparable with the combinations of interstitial broncho-pneumonia with patches of lobular pneumonia in the streptococcal infection, in which, although the streptococci have been restrained for a long time, they finally thrive in certain patches of the newly sensitized tissue.

Although it is possible to distinguish the forms of pneumonia caused by the invasion of different bacteria in tissue prepared for their reception by predisposing disease, the nature of the predisposing diseases measles and influenza remains obscure.

A PSYCHO-THERAPEUTIC CLINIC IN THE JURA MOUNTAINS

By C. F. Martin, M.D., Montreal

IT is a far cry from the mysteries of Osiris and Eleusis to the more patent quasi-religious miracles of Notre Dame de Lourdes, and from the healing powers of the "Divine Physician" to the days of modern occultism. Each era throughout the centuries has had its miraculous healers of disease, and each exponent has had his hordes of adherents. Just as the Roman emperor Caracalla worshipped Apollonius of Tyana, who is virtually the spiritual progenitor of Mary Baker Eddy, so did the nobles of mediæval times bow before the quasi-quackery of Paracelsus and Mesmer, and to-day the devotees of various occult but unorthodox methods of healing are numbered by legions, be they Christian Science, Mental Science, Osteopathy, or Chiropraxy.

And thus the miracles, so called, have been in operation since time immemorial, more often under the guise of mystery than of science, while all the time the fundamental underlying factor lay simply in a faith in the power to heal, and the influence of suggestion that makes for health, and so the quasi-religio-medical masquerade has continued throughout the ages. Fortunately, as in other great movements, so with these, the underlying germs of truth lived on, until to-day psychology and rational medicine have recognised the essential difference between organic and functional disease and the predominance in the symptoms of the functional factor.

Never has such a stimulus been given to this revival of interest in the so-called occult healing as during the present war, and the various methods of curing functional disease have been called to the aid of suffering humanity. Pre-eminent amongst these various methods of suggestion there stands out to-day not only the use of hypnotism, but most of all the employment of persuasion, education, and ex-

planation. In all the more important warring countries neurological centres have been established, which have busied themselves with the treatment of functional nervous disorders. None of these is more impressive than that in the Jura Mountains, visited during the summer of 1918.

The ancient city of Besançon, a capital city in the time of the Gauls, and known to the Romans as Vesontio, possesses in the Hospital of St. Jacques a distributing centre for the convoys of nervous cases brought from the forward areas of the eastern battle zones of France. Situated in the foot-hills of the Jura Mountains, with its picturesque citadel built under the direction of the famous strategist Vauban in 1664, and with its interesting ancient Roman monuments, it forms one of the most delightful clinical centres of the war zones. Under the skilful guidance of Dr. Roussy, soldiers with all manner of nervous diseases are admitted and examined, and from this "triage," or distributing centre, the functionally disordered patients are sent south for treatment to the psycho-therapeutic centre at Salins. The dull little town—about 50 kilometres from Besançon,—is reached by one of the most picturesque roads in all Europe, and the pilgrimage thence, along the valleys of the Doubs and the Loue, should bring one, in itself, a contentment of mind even before the destination is reached, viz.: the Psycho-therapeutic Hospital, located in the historic fortress of St. André.

This well-preserved monumental fortress, 2000 feet above the level of the sea, likewise testifies to Vauban's skill, for the fortress dominates the surrounding country, looking out upon the southern and eastern borders of Switzerland and Italy, a defence against prospective invasion in the seventeenth century. The town, itself, with its great salt beds, and its Établissement des Bains, erected by Grimaldi in 1855, has been visited as a health resort from time immemorial, and to its saline and sulphur springs, as well as to its climate, have already been attributed wonderful healing powers.

One may drive by a wide and winding road, as do the ambulances, to the Fortress Hospital, or one may follow the example of the more energetic staff and climb the steep but narrow path, leading by a shorter course, to the mountain top. On arrival at the Fort one crosses the moat by the usual bridge to find, on entering

the enclosure, a wonderfully preserved type of fortification of the reign of Louis XIV: so complete in its architectural design, and so solid in its structure as to have been used for its original purpose down to 1888, when modern methods of warfare rendered it unsuitable for other purposes than a garrison. The larger rooms of the fortress form the wards of a hospital, while the smaller ones are the offices, museums with their exhibits, and cinematographic shows.

Nowhere in France is to be seen such a concentration of functional diseases, nor will one see anywhere more satisfactory results. Paralysis of the extremities in all their weird varieties, hysterical paraplegias, hemiplegias, and monoplegias, soldiers with astasia-abasia; others again with contractures that have been present for years; some with "plicatures," their vertebral columns bent forward, others in a position of scoliosis—some with neuropathic pseudo-coxalgia, others again with wry necks; and so on *ad infinitum*. Here, too, one saw for the first time the "Marseilles thumb," an adduction, first occurring in a soldier belonging to a regiment from that ancient city, and later by contagion of ideas, occurring in numberless recruits from the same source. Here, too, was seen the obstetrical hand, the *main figée*, likewise the reflex neuroses, whatever their origin, conditions all cured more or less speedily in quasi-miraculous fashion.

Not less interesting in other wards were soldiers with unusual tremors and pseudo-choreic movements, resulting from emotional disturbances of war. The commoner psychosensory disturbances, the defects of speech and hearing and of sight, all of these in varying degrees, were likewise amenable to the skilful treatment there employed.

And lastly is the group of self-inflicted lesions—more especially the extensive œdemas resulting from ligature—which, of course, require treatment of an entirely different character.

It is of intense interest to note by what methods Roussy and his assistants have effected their cures. Treatment by psychotherapy is too much a matter of commonplace in every neurological centre of Europe and England to be dealt with here in detail. Suffice it to say that the methods differ widely and the approach to the patient depends very largely on the attitude of mind of the physician. In

one clinic at Beauvais, incarceration in a dark room under severe privations was resorted to as a disciplinary measure, usually with rapid success. Patients who refused to get well promptly were returned to their cells until such time as the fear which had induced the disease was dominated by the greater fear of its treatment. In other clinics, again, the method of *torpillage* was adopted with signal success; this consisted in the administration of powerful currents of galvanism, inasmuch as, forsooth, faradic electricity was not considered sufficiently severe. Nevertheless, in most centres the less drastic, but withal powerful faradic brush has proved sufficiently efficacious, and succeeding treatments either demonstrated the possibility of movements in disordered limbs or, again, established a fear greater than that which had previously limited their function.

Still more humane measures were adopted in many centres by isolation in cubicles, and with milk diet, the object desired being attained through rest and discipline. In the Centre at Salins, however, these severe methods of suggestion and discipline are deprecated, and the key-note of the treatment is kindness, persuasion, and education. New patients are placed at rest in comfort for a few days after admission, and are then allowed to circulate among those whose cures are already established or in progress, and thus a contagion of health and healthy ideas is encouraged; so much so, indeed, that often before the treatment is commenced, the need for it has almost disappeared. Not infrequently, indeed, gentle faradism is applied, rather with the object of demonstrating in contractures or paralysis that muscles are still able to functionate and not with the idea of causing unnecessary pain or inculcating discipline. The absence of other means of treatment, of elaborate appliances with massage and electrical devices becomes very impressive, and it is interesting to note how at the Seale Hayne Hospital in England, the same brilliant success is obtained by similar methods and along the same ideal lines under the skilful guidance of Colonel Hurst and his associates. Here, as at Salins, the atmosphere is one of kindly interest and rational therapeutics.

There are many interesting demonstrations of the successful treatment at the Fortress hospital in the museums there established: the numberless crutches, splints, and plaster appliances,

thrown aside because found needless, testify to the importance of proper diagnosis and psycho-therapeutic treatment.

A small hut erected in the porter's grounds is devoted to the cinematograph—not for the amusement of the patients, but to demonstrate in a series of graphic films the progress in treatment—the improvement in the movements of affected limbs from the inception of the disease to the period of complete restitution.

As in former ages then, so to-day the performance of miracles continues, with this difference, that this more modern practice, while less dramatic though equally effective, is based upon the principles of science and intellectual honesty.

THE LIFE CHART AND THE OBLIGATION OF SPECIFYING POSITIVE DATA IN PSYCHOPATHOLOGICAL DIAGNOSIS

By Adolf Meyer, M.D., Baltimore, Md.

IN his address at the opening of the Henry Phipps Psychiatric Clinic, Sir William Osler told the following charming anecdote: "I found a big West Virginian in the private ward one morning. The history was colorless. I went over him thoroughly. 'There is nothing the matter with you,' I said. 'I didn't say there was,' came the reply; 'that is what I wanted to know.'"

In quite a few similar cases one might raise the question: How, then, did the patient come to have doubts about his health? Many a so-called neurotic leaves the physician without what really ought to be an obligatory accounting for the solicitude or worry.

Sir William Osler continues: "We are all a bit sensitive on the subject of our mental health, but a yearly stock-taking of psychic and moral states under the skilled supervision of a competent reviewer and interpreter of human problems and assets and their best management would be most helpful to most of us." He gives a few diagnosis slips:

"Mr. J. A. A tendency to irritability of temper.

"Mrs. R. Too much given to introspection.

"Miss B. Overanxious about her soul.

"Master G. Worried by a neurasthenic mother."

These are, indeed, good samples of problems presenting themselves, and I feel that, if we are able to specify perfectly objective facts in terms of definite situations and reactions plainly inviting adjustment and action, there would be little cause for sensitiveness.

The two big sins of the physician against the psychoneurotic are apt to be the dismissal of the patient with, "Nothing the matter with you" (with perhaps a hint that he or she had best go to Christian Science or to some cure-all), or the statement: "What

I find is enough to account for all your nervous symptoms." Either statement is apt to encourage neglect in the examination of the psychopathological and the situational status of the patient. Well-directed attention to these settings will make the verdict safer for the patient, and ultimately also do better justice to the responsibility of the physician.

How, then, can we pin down the pertinent facts? How can we get them into a form which will be a safe, dependable formulation in terms of an "experiment of nature," or of a problem of functional pathology, suggesting more or less well-defined non-derogatory therapeutic modifications?

Medical psychology consists largely in the determination of the actual life-history and experiences and concrete reactions of the patient, and the gaining of a safe and sensible perspective, so as to adapt as far as possible the aims to the means and the means to the aims, and the personality to the situation and the situation to the personality.

The facts which really count are as plain and tangible and concrete and controllable as those in any other part of the record and examination of the human being. Unfortunately, they may be unwieldy, and form a "long story," and before we can say that we have a clean-cut and practically useful view of the fateful bias indicated by the history, it must be shown by careful scrutiny of the facts that the allegations tally with what the person actually shows objectively by behavior and associations and with the history furnished by the friends. It is the length of the records and their apparent lack of pointedness that make many physicians shun the task. It is, furthermore, somewhat difficult to control the time relations and causal interdependence of the events.

To facilitate a concise final review of the facts, I use a device which, I hope, illustrates not only our practice, but also the entire philosophy involved in it.

The patient who comes to the physician is naturally examined, not only for the history and present condition of each organ and function, but also for the development and condition of the integrated personality. In order to record the facts in a graphic manner, we can use a life record for each of the principal organs, giving sufficient space for each year so that we can record dates

Year:		Birthday: Jan. 11, 1895.	Yr.
1896		Youngest of 17. Mother—second wife. Learned to walk and talk in the first year.	1
1897	Cholera Infantum		2
1898	Broncho-pneumonia		3
1899	Croup	Well developed; large for his age.	4
1900	Usual exanthemata		5
1901			6
1902		Began school.	7
1903		Open disposition; friendly, but quiet.	8
1904		Preferred staying at home to playing with others.	9
1905			10
1906	Autoerotism continued to present (1916).		11
1907	Malaria	No worries.	12
1908		Only close companion a cousin of own age—very wild boy. Intimacy continued to present time (1916).	13
1909		Dredge-hand in boat of brother-in-law. Left school (7th grade).	14
1910		Industrious, saving money.	15
1911		Bought boat. Crabbing, dredging oysters. { Summers at home. Winters in Balto. with brother.	16
1912		Quarrels with brothers; thought he was abused, being the youngest.	17
1913	Illicit relations. Neisser infection.	Went with girls often, but no serious love affairs.	18
1914	Autoerotism increased		19
1915	Depression	Feb.—Refused admission to lodge; kidney trouble. Depressed; stopped work; worried over illness. At home.	20
1916		Worked 6 weeks. Unconscious in boat (Aug.) Peculiar words and behaviour. Reproached sisters for immorality. Hears voices; uneasy; frightened; then dull. At home.	21
1917		Development of semi-stupor and indifference. Entered Clinic.	22

FIG. 1. HEREDITY, PATERNAL UNCLE ALCOHOLIC. MATERNAL GRANDFATHER INSANE. ONE BROTHER HAD TWO DEPRESSIONS.

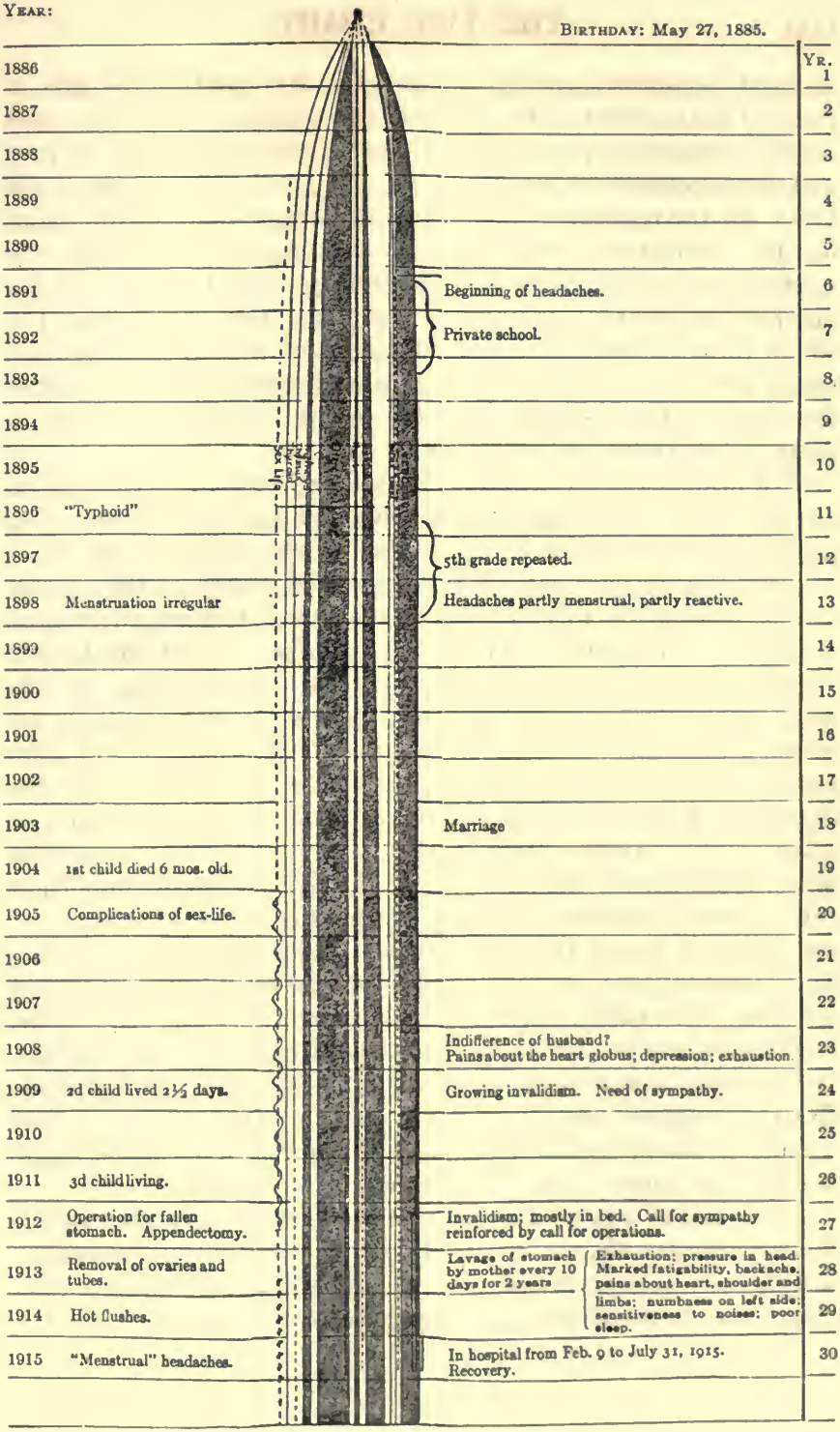

FIG. 2. CASE OF INVALIDISM.

at least accurately enough to indicate the months. To give a rational background to the scheme, the weight-curve of the most readily comparable part of each system is charted. For the nervous and mental conditions we use the growth curve of the weight of the brain; for the respiratory apparatus, the weight-curve of the lungs; for the circulation, the heart; for the digestive apparatus, the weight-curve of the liver; and similarly we add the curve of the kidneys and that of the thyroid, thymus, and sex glands. The whole forms a tracing of the life-curve of the entire organism, whose integration in its relation to the environment then becomes the basis of the so-called "mental record," which is entered in terms of situations and reactions.

We begin with the entering of date and year of birth so as to be able to read off easily the individual age and the corresponding calendar years (the age being entered on the right and the years on the left); we next enter the periods of disorders of the various organs, and after this the data concerning the situations and reactions of the patient. The space on either side of the tracing of the organism is used for explanations, but especially for the data which constitute the principal situations and reactions expressing the "mental" record, permitting various degrees of completeness. On the right border near the edge we may note the changes of habitat, of school entrance, graduations or changes, or failures; the various "jobs"; the dates of possibly important births and deaths in the family, and other fundamentally important environmental incidents. Nearer the middle of the free space to the right one enters the more personal psychobiological and practical reactions, such as the beginning and development of dominant interests, friendships, etc.; the occurrence of special difficulties, including minor peccadilloes, such as confabulations, lying, stealing, and various temptations, and the duration of their influence. Brackets indicate the duration of some of these features. Any specific trends of special importance in the evolution of the illness had best be underscored with different-colored inks.

It is well to put on the left side the entries concerning special diseases, the sex life, etc. In case that the details of illnesses require more space, certain periods can be charted on a supplementary chart so as to make the spaces represent months instead of years.

The two accompanying examples will explain the plan better than would extended description.

The first chart presents the data of a patient with schizophrenia. The second gives the facts in a case of invalidism in which a recovery might possibly have been obtained without mutilation.

In the latter case you find from the age of five a habit of headaches, a dependence on others, lack of emancipation, a tendency to appeal for sympathy by her complaints; then after her marriage and the birth of a child and subsequent interference with her normal instinctive life, fear of losing the affection of her husband (a friend of the wife had come to live in the house), and more invalidism; then several unfortunate and mutilating operations, a real evisceration without any evidence of a study of the facts in the case, but finally a readjustment under a treatment reestablishing better habits, a better understanding of the difficulties, and an end of making the remaining organs, the stomach and the head, the scapegoats for the failure of adaptation.

This brief note may illustrate the objective practical procedure of modern psychopathological studies, and how simply, controllably, and suggestively the facts can be brought into a record.

PNEUMONIA AND EMPYEMA AT CAMP DODGE, IOWA

By Lt. Col. Jos. L. Miller, M.C., Chicago, Ill.

During the year preceding September 20, 1918, approximately 800 cases of pneumonia entered the Base Hospital at Camp Dodge. This does not include upward of 2000 cases that developed shortly after this during the influenza epidemic. These pneumonias may be divided roughly into three groups. Ordinary lobar pneumonia, in all 276 cases from September 20, 1917, to March 20, 1918; 400 streptococci pneumonias from March 20, 1918, to May 10, 1918; and 125 lobar pneumonias from May 10, 1918, to September 20, 1918.

During the autumn of 1917 a very mild type of pneumonia prevailed, as indicated by a mortality of 7 per cent in the first 100 cases. During the winter the infection became more virulent, the mortality in the total of 276 cases being 11.27 per cent. In the first 88 cases terminating by crisis, the duration in 7 was two days; in 11, three days; in 13, four days; 13, five days; 18, six days; 9, seven days; 10, eight days; 2, nine days; and 5, ten days or more. The colored troops, which made up about one-sixth of the strength of the command, made up 116 of the 276 pneumonias.

The various pneumococcus types were as follows: I, 22.87 per cent; II, typical and atypical, 46.8 per cent; III, 7.6 per cent; IV, 22.8 per cent.

Inasmuch as all of the pneumonia patients entered the hospital early, while the infection was still localized, and as all were *x*-rayed within twenty-four hours, the lobe where the infection began was quite accurately determined. In 596 cases of both types where the infection still was localized the lower left lobe was involved in 253; lower right 252; upper right 45; upper left 23; middle 13; entire right lung 5; entire left lung 1; and in both lungs 5.

The lobar pneumonia presented the usual symptomatology. The only point of interest was the gradually increasing virulence, as manifested by the mortality from October 1, 1907, to January 1, 1918, and the gradually increasing frequency of empyema. In October this complication appeared in 2.3 per cent of cases; in November, 2.2 per cent; in December, 17.3

per cent, reaching its maximum in January with 27.9 per cent. Empyema was further characterized by loculated pus pockets, which accounted for the high mortality. This made diagnosis extremely difficult; although the standing orders were to have each patient *x*-rayed every five days and frequent exploratory punctures were made, several patients came to autopsy with undetected pus pockets. The *x*-ray, when frequently repeated, was of considerable value in detecting an exudate, although the differentiation between fluid and consolidation was not definite. One of the distinct values of the *x*-ray was to stimulate careful physical examination by the Ward Surgeon.

The epidemic of streptococcus pneumonia appeared suddenly between March 18 and 20, 1918, and continued with great severity for six weeks, then gradually subsided, although the epidemic was not actually over until June 1, 1918. After the first three weeks, however, the virulence of the epidemic became less marked. This should be emphasized when considering the various therapeutic measures employed. At the onset of this epidemic it was recognized by all the medical officers that this was different from the pneumonia they had seen in civil life. Severe intoxication appeared very early, the disease frequently running a very rapid course: Lobar dullness and lessened respiratory sounds were the rule; but typical bronchial breathing was very infrequent. In addition to the area specially involved, scattered moist, fine râles were frequently heard over various parts of the lung. Rusty sputum was frequent but not constantly present. While autopsy revealed that we were dealing with broncho-pneumonia, inasmuch as the process usually became confluent in one or more lobes, from a clinical standpoint, it would have been diagnosed as lobar pneumonia. Empyema developed with great frequency and was very difficult to detect on account of the absence of bronchial breathing and the presence of suppressed breath sounds even in the absence of fluid.

Of the various unusual findings the great frequency of empyema was the most striking, as it developed as a complication in 34.8 per cent of all the streptococcus pneumonia. It was most frequent in the white troops, 42 per cent as compared with 26 per cent in the colored. Multilocular collections of pus were very common, occurring in the interlobar spaces, adjacent to the mediastinum, posterior to the sternum and as lung abscesses. Suppurative pericarditis was found in 34.8 per cent of empyemas coming to autopsy, or a total of 38 cases. It was associated with right-sided empyema 11 times, left-sided 18 times, and bilateral empyema in 11 cases. Suppurative pericarditis was found only twice in colored soldiers.

Suppurative peritonitis was present in 17 of the 109 empyemas coming to autopsy. The empyema was right sided in 8, left in 5, and bilateral in 4.

In 6 of the 17 cases there was a combination of peritonitis, pericarditis, and empyema.

Other complications occurring with relative infrequency were: Arthritis 8 cases and erysipelas 5. Acute endocarditis and gangrene of the lung was found only once. Suppurative otitis media was quite common, but exact figures are not available.

Empyema was much less frequent among the colored soldiers, developing in only 20 per cent of the cases as compared with 45 per cent among the whites.

The mortality of the lobar pneumonias was 11.2 per cent, of the streptococcus pneumonias 32.5 per cent. The deaths from uncomplicated streptococcus pneumonia was 10.7 per cent in the whites, and 19.9 per cent in the colored soldiers. The mortality of the empyemas occurring with so-called pneumococcus pneumonia was 52.5 per cent. With empyema occurring during the streptococcus epidemic 60.4 per cent. The mortality was lower in the colored soldiers—44 per cent as compared with 64.8 per cent among the whites.

The treatment of the pneumonia, all types, was fresh air, with morphine to relieve pain and give sleep and rest; tincture of digitalis, beginning with 1 c.c. every three hours day and night at the onset of the trouble, and continuing this dosage throughout the course of the disease unless evidence of intoxication appeared. No attempt was made to reduce temperature by bathing. The Rockefeller serum was not used, and in the 276 cases of lobar pneumonia only two patients died from "type I" infection.

The empyemas developing as a complication of the 276 lobar pneumonias were treated by rib resection. At the onset of the streptococcus empyema, immediately upon detection of a turbid fluid containing streptococci, drainage under local anesthetics by rib resection was performed. The results were not satisfactory. Many patients returned from the operating room in a state of shock from which they did not recover. In their extreme toxic condition, apparently the shock of the operation, and especially the effect on the heart of the artificial pneumothorax, was sufficient to at least hasten a fatal termination. After employing this method of treatment for about ten days, a change was made to repeated aspirations until the condition of the patient was sufficiently improved to warrant operation. The results from this procedure appeared to be much better; in fact, the improvement was so marked in some of these cases after a few aspirations, that the operation was delayed and 11 cases recovered without operation. Six of these were aspirated only once. It is possible, and perhaps probable, that these would have recovered without aspiration.

When we compare the mortality results of these various methods of treatment, it is noted that in 43 cases with early operation, 52.5 per cent died. In 49 with repeated aspiration, then operation, the mortality was 32.5 per cent. In 56 cases aspiration alone was performed either because the improvement was so marked after aspiration that an operation was not considered necessary, or because the patient's condition was so grave that an operation was unwarranted. Forty-three, or 75.7 per cent., of this group died.

One point should be considered in regard to these figures, viz. that apparently the virulence of the infection was more marked early in the epidemic. Immediate operative measures during the first three weeks of the epidemic gave a mortality of 52.5 per cent, while immediate operation later in the course of the epidemic gave a mortality of 28.6 per cent. The difference in mortality from the two procedures is probably in part at least only apparent, and can to a considerable degree be explained by the difference in virulence at the two periods.

CLINICAL OBSERVATIONS ON THE LATE PULMONARY EFFECTS OF GASSING

By Roger S. Morris, M.D., Cincinnati, O.

Lieutenant Colonel, Medical Corps, U. S. Army, A.E.F., Germany.

IN the Hun's display of frightfulness during the Great War, nothing which he has exhibited to the civilized nations of the world has more clearly shown his utter lack of a sense of honor —of "playing the game" in a sportsmanlike manner—than his treacherous and cowardly introduction of poisonous gases in warfare. When he launched this weapon, a new and extremely urgent clinical problem was presented on a vast scale to the Medical Corps of the Allied Armies. The situation was wholly unexpected and without precedent, and the agony and suffering and the resultant loss of life have been untold.

With the acute effects of poisonous gases we need not here concern ourselves. It is happily a closed chapter, which, there is every reason to hope, will never be reopened. Unfortunately, however, the clinical course is frequently not ended with the subsidence of the symptoms of acute poisoning. It is with the later effects of poisonous gases that the present notes are concerned.

It has been pointed out by Professor Achard,[1] in an analysis of 2218 gassed cases (561 of suffocating gases, 1657 of mustard gas), that suffocating gases (chlorine, phosgene, etc.) are much more apt to lead to chronic indispositions than is mustard gas. He found 195 patients suffering from the late effects of suffocating gases. The decision as to the nature of the gas was, however, often difficult, as mixtures of gases were so frequently employed. Among the patients who had been gassed with suffocating gases, 93 were observed within six months, 54 within six to twelve months, 41 between one and two years after gassing, and in 7 the symptoms had persisted more than two years. With vesicating gases, on the other

[1] Lecture delivered by Professor Achard at Paris, October 9, 1918, to members of the Medical Corps, United States Army.

hand, there were only 3 cases in whom the symptoms persisted beyond ten months.

As Professor Achard emphasized, the symptoms of gassed patients are often those of pulmonary tuberculosis, and it is with this group that we are here chiefly concerned. In another connection, Thomas Lewis and others have also drawn attention to the fact that the effort syndrome, in its symptomatology, is indistinguishable from pulmonary tuberculosis and various other organic diseases. It is only by means of objective examination that the differentiation is possible.

In order to limit the present communication, only those gassed patients complaining of hemoptysis are considered. It is here that the question of a tuberculous lesion will most frequently arise. It may be added in passing that the history so frequently indicated a mixture of mustard gas with suffocating gases that we have not attempted to differentiate between the two.

Hemoptysis has been found to be a relatively common late symptom after gassing. The majority of our patients were wounded with gas within the last six or eight months (February, 1919), and it is not possible, from our own observations, to state how long this symptom may persist. Patients gassed at Château-Thierry in June, 1918, are still spitting up blood in February, 1919. It is quite evident, from the experience of the French, that we will have numbers of soldiers in whom the symptom may be present months after their return home.

The amount of blood expectorated is generally small. Most frequently the sputum is only blood-streaked, though at times the patient describes clots representing a teaspoonful or more. In this group of patients, other symptoms also may strongly suggest pulmonary tuberculosis. Chronic cough is common, usually worse in the morning. There is apparently nothing characteristic in the appearance of the sputa. Night sweats are frequently complained of, often so severe that the clothing is saturated with moisture. Weakness and dyspnea on exertion are almost always present, greatly limiting the activities of the patient. Tachycardia and palpitation on exertion are common. Vertigo is not infrequent. Among our patients we have encountered very few with evening elevations of temperature to 101° F., such as Achard describes. Generally the

temperature has been normal, or there have been rises to 100° or less. Loss in weight, amounting to 5 to 10 pounds or a little more, is common.

Pain in the chest has been a frequent symptom among our patients, for which it has rarely been possible to detect a physical basis. It is usually dull in character, though occasionally sharp, and is nearly always produced or aggravated by deep inspiration or by coughing. A history of preceding inflammatory disease of lungs or pleura is by no means the rule. A recent patient, however, presented findings of some interest.

He had had pneumonia in 1902 and was critically ill. A needle was introduced into his left axilla at that time, and fluid was withdrawn. He made a complete recovery and was entirely well, except for a second attack of pneumonia in 1909, until he was gassed last August. Since then he has suffered with pain, dull in character, in the lower left axilla, whenever he takes a deep breath. A radiogram shows a band of adhesions between the left chest wall and the diaphragm; fluoroscopic examination confirms this finding. Asked, during the latter examination, to indicate where he felt pain, the patient placed his finger directly on the point of attachment of the adhesion to the chest wall.

The findings in this patient suggest the possibility that similar pains may be associated with adhesions, which escape detection. The physical findings in the majority of our patients have been normal. That is, there is not usually dullness or retraction of the apices, and it has been unusual to find râles, even after cough and deep inspiration. In a few instances, however, we have noted râles persistently in one or both apices. It is in the patients with râles and hemoptysis particularly that pulmonary tuberculosis would seem altogether probable, and yet our experience, though less extensive, coincides with that of Achard, in that repeated examinations of the sputa fail to reveal tubercle bacilli.

The differentiation of pulmonary tuberculosis and the late effects of gas is also greatly facilitated by *x*-ray examination, as Achard again has shown. One fails to find the evidence of infiltration of the lungs in gassed patients. A change which occurs with great frequency, however, is an increase in the density of the hilum shadow, which tends to assume a form more or less oblong. It is not pathognomonic, but is very suggestive of gassing.

There is a smaller group of patients, of whom I have seen only a few examples, in which the clinical picture is that of advanced tuberculosis of the lungs. Here, the patient is iller, there is cough with profuse muco-purulent or purulent expectoration, frequently hemoptysis, fever to 102° to 104°, with morning remissions, sweats, emaciation, and great prostration. The clinical condition is precisely that of advanced pulmonary tuberculosis, and the issue may be fatal after a period of months. Such a case was seen on the service of Major J. B. Whinnery at American Red Cross Military Hospital No. 5 at Auteuil.

The patient, severely gassed in August, had been confined to bed continuously till his death in November. The physical findings during the latter part of his illness were those of advanced phthisis of both lungs. Repeated examinations of the sputum were negative for tubercle bacilli. At autopsy, no evidence of pulmonary tuberculosis was found. There were marked bronchial and peri-bronchial thickening and an extensive acute broncho-pneumonia, superimposed on a more chronic inflammatory process with fibrosis.

The milder symptom complex is one which will be encountered frequently in civilian and military hospitals in Allied countries. The importance of recognizing its etiology and of differentiating it from pulmonary tuberculosis is obvious from several points of view. In the first place, the prognosis in the gassed patients is altogether good. The majority recover within a year, according to Achard's figures; few persist beyond two years. Furthermore, the patient and his family should be spared the mental worry which pertains to a diagnosis of tuberculosis.

From the standpoint of the governments concerned, the separation of this group of patients from the tuberculous is also important in relation to pensions, war risk insurance, etc. There is no reason to anticipate at present that the gassed patient will continue indefinitely to be a burden upon the State, while the reverse may hold good in a large percentage of the tuberculous.

Summarized briefly, a history of chronic cough, hemoptysis, weakness, sweats, slight fever, loss in weight, in conjunction with a history of having been gassed, indicates the probability of a non-tuberculous condition, the result of the gassing. The differentiation from tuberculosis is made by the absence of tubercle bacilli from

the sputum and by the lack of *x*-ray evidence of tuberculosis. Physical examination of the lungs may be very suggestive of a tuberculous lesion, and too much importance should not be attached to persistent râles.[2]

[2] Owing to four months' delay in transmission, due to faulty address, the invitation to contribute to this volume was only received February 14, 1919, while stationed with the Army of Occupation in Germany. The necessity of having the manuscript in Washington by March 20th has precluded the possibility of referring to the literature and has necessitated haste in preparation. It is felt that a brief word of apology for this fragmentary, incomplete note is due, for one's best would be all too little to offer to the great and beloved physician, who has given so abundantly to his students.—R. S. M.

THE DIAGNOSIS OF TRAUMATIC HEMOTHORAX

By Geo. W. Norris, M.D., Philadelphia, Pa.

IT would seem at first sight that the physical signs of traumatic hemothorax or hemopneumothorax would be identical with those due to pathological causes. This, however, is by no means the case, and hence it frequently happened during the recent war that erroneous diagnoses were made. This article, which is based upon the personal observation of many hundred penetrating or perforating wounds of the chest, is written with the object of setting forth what appear to the author to be the most important points to be borne in mind. In order intelligently to interpret physical signs it is necessary to form a mental picture of conditions within the chest. Some of the possibilities may be mentioned.

1. A high-velocity bullet may have perforated the chest, causing only minute wounds of entrance and exit, associated with but little bleeding, pneumothorax, or pulmonary collapse.

2. A shell fragment may be lodged in the lung, which has bled profusely into the pleural cavity; (*a*) there may be free air, free blood and a collapsed lung; or (*b*) there may be little or no free air, a large hemothorax and a compressed lung, the latter being Nature's usual method of checking hemorrhage.

3. The superficial wound may be large, with extensive comminution of the ribs, and the wound of the (air) "sucking" variety. This type being usually associated with marked mediastinal displacement, dyspnea, shock, and ultimately, if the patient survives, infection.

It is well to remember that in all three types the diaphragm is always high even when considerable blood has flowed into the pleural cavity. There are thus always four possible causes for tympany on percussion, which is a very frequent finding; i.e. (*a*), free air, (*b*) relaxed lung, (*c*) high abdominal viscera, (*d*) gas bacillus infection.

Mediastinal displacement is very common, and it is particularly to be emphasized that abnormal physical signs on the uninjured side, especially posteriorly, are of very frequent occurrence. The mistake most commonly made by the novice is to diagnosticate a pneumonia either on the wounded or unwounded side, when none exists. Pneumonia as a complication, especially an early complication, is unusual, not to say rare; whereas the physical signs of pneumonia are quite common. The presence of fever and leucocytosis is of little aid in differentiation, as they may readily be due to wound infection.

As in civil practice, it is usually impossible to demonstrate by physical signs a pleural effusion of less than 400 c.c. The *x*-ray is often equally useless as a diagnostic aid for small effusions, especially if the patient is on his back.

Hemothorax with or without atelectasis either on the injured or the opposite side may exist without actual penetration of a missile.

I. *The History.* A man whose lung has been wounded usually falls to the ground, frequently suffers from immediate severe dyspnea, and as a rule either at once or within a short time spits up blood. The mere fact that he was able to walk or crawl a mile or more (usually with frequent halts) is no indication that he has not suffered severe pulmonary damage.

II. *Inspection.* Dyspnea of varying degree, with unilateral diminution of thoracic movement, often associated with pallor and bloody expectoration, are the usual phenomena. If the lesion is right-sided, a visible displacement of the cardiac impulse is the most striking and diagnostically important feature, indicating not only a pleural effusion, but suggesting a considerable amount. It must not be forgotten, however, the left-sided pulmonary collapse, which may be contralateral, and which may occur simply from contusion without penetration, may be deceptive. Such collapse, although rare, has been demonstrated both radiographically and at autopsy. Contralateral atelectasis must not, however, be invoked to explain physical signs unless other causes can be eliminated with reasonable certainty. Cardiac displacement to the right from a left-sided hemo- or hemopneumothorax is less easy to determine by inspection of the cardiac impulse alone, although diminished respiratory motion is usually found.

III. *Palpation.* Except as an aid in locating the position of the heart, palpation has usually less value than the other classical methods of examination. As a rule fremitus is diminished over the effusion and increased over the unaffected side. If the lung behind the effusion is markedly compressed, fremitus will be present, as is the case in the pathological effusions of civil practice.

IV. *Percussion.* The frequent occurrence of tympany, and the possible causes thereof, have already been pointed out. Such tympany is usually quite readily differentiable from the hyper-resonance encountered over the sound, vicariously functionating side. Quite often, especially if the patient has been lying on his back, the whole anterior and lateral aspects of the chest may be tympanitic and only posteriorly will dullness be demonstrable. It is often quite impossible to outline the cardiac dullness on one or the other side owing to the presence of such tympany. Not infrequently Grocco's area of triangular dullness can be demonstrated, especially in large hemothoraces. Frequently this will be associated with bronchial breathing on the uninjured side, a physical sign which may result from mediastinal displacement, either with or without compression of the sound lung. Such bronchial breathing is often mistaken for pneumonic consolidation. Movable dullness is sometimes demonstrable, especially if free air is present, but as a rule the blood is too clotted, and the pleural cavity too full of blood and lung to permit of much, or of a rapid gravitation of blood. Nor is the demonstration of movable dullness worth the trouble its demonstration entails.

V. *Auscultation.* Associated with the increased respiratory excursion which one sees on the sound side, the breath sounds are harsh, exaggerated, and variably associated with râles. The sounds are often so loud that they are transmitted to the injured side, where, especially below the clavicle, they may give the impression that the upper lobe is functioning, whereas this lung may be atelectatic or completely compressed. When in doubt in this regard, the degree of motion of the injured side and the amount of cardiac displacement will often make the situation clear. Bronchial breathing, whether heard over the sound or the injured side, will nearly always indicate compression, and but rarely pneumonic consolidation. Amphoric or cavernous breath sounds, generally associated with whispered pectoriloquy, point to hemopneumothorax and are often heard over

chests with sucking wounds or after drainage tubes have been introduced.

Friction sounds are generally present and result from the sticky fibrinous moiety of the outpoured intra-pleural blood. The testing of vocal resonance by means of whispering is preferable to speaking, inasmuch as it is less taxing to the patient.

VI. *Exploration.* A good-sized exploratory needle and a reliable syringe should be unhesitatingly, freely, and repeatedly used, not only for the purpose of demonstrating a hemothorax—which, if small, is of minor importance—but of determining the presence of infection, especially infection by a gas-producing organism. It is to infection that practically all the late fatalities are due. One must bear in mind that infection is often localized, and that although a single exploration may yield a sterile culture, another puncture only a few inches away may reveal virulent organisms. As a rule the blood contained in the pleural sac is clotted, and needling at the angle of the scapula often yields a "dry tap" at a time when large quantities of liquid blood can be withdrawn high up, anteriorly or in the anterior axillary line. The high position of the diaphragm which has already been alluded to must be borne in mind when exploratory punctures are made.

When blood has been poured out into the pleural cavity, it after a time separates into two parts: (*a*) a thick, fibrinous corpuscle-enmeshing portion which accumulates posteriorly, especially at the base; takes a long time to absorb; forms adhesions; and is accountable for the persistent percussion dullness which lasts long past the usual convalescent period; and (*b*) a thin, dark-red or brownish-red fluid, which collects anteriorly and laterally, and constitutes the "blood" which is withdrawn when aspiration is performed.

It is usually advisable on the third or fourth day after the injury to remove as much of the outpoured blood as possible. Secondary hemorrhage is usually small in amount, and the removal of large effusions markedly shortens the period of convalescence, and gives great mechanical relief to the respiratory and cardiovascular functions.

Infected Hemothorax. The chief function of the physician in such cases as have been discussed lies in the early detection of infection.

If infection can be avoided, the vast majority of patients who reach the Evacuation Hospital will ultimately recover.

A persistent or increasing temperature or pulse rate are the most reliable indices of an infected hemothorax. The possibility of its loculation and the importance of frequent needling have already been alluded to. Constitutional signs such as anorexia, restlessness, increasing pallor, insomnia, are important signs but usually rather late manifestations. A sudden increase in tympany, cardiac displacement, and the appearance of (often deep) jaundice point strongly toward gas bacillus infection and indicate immediate resection and drainage.

A point which is often perplexing, of which the solution is chiefly a matter of individual judgment and experience, is the decision to operate or not to operate against the dictates of bacteriological findings. Not infrequently a patient will show steady improvement, absence of constitutional symptoms, and a practically normal or constantly declining pulse rate and temperature, while the laboratory reports organisms microscopically or growth on culture media. In such cases it is often best to wait further developments, remembering that the infected area may be walled off and that recovery may take place without having to subject the patient to the prolonged and trying convalescence which a thoracotomy entails. If such a course is pursued the patient must be assiduously watched, and the physician should be fully aware of the responsibility he has assumed. This applies, although with great rarity, to cases in which gas-producing organisms have been reported. As a rule, however, the presence of a gas bacillus is an absolute indication for immediate operation. There are, on the other hand, cases in which, despite negative bacteriological findings, rib resection should be performed. A fetid odor of the aspirated blood also points most emphatically to surgical intervention, but one must not be misled by the stale, mawkish odor which old blood often possesses even when it is culturally quite sterile and innocuous. After all is said and done one's decision will be markedly influenced by the confidence one has in one's bacteriologist.

Abdominal Signs and Symptoms. Injuries of the pleura, especially when in the neighborhood of the diaphragm, often give rise not only to abdominal pain and rigidity, but also to nausea and vomiting.

These facts are important for the obvious reason that one frequently has to decide whether the missile which entered the pleura has penetrated the diaphragm, perforated a viscus, or set up a peritonitis. Needless anesthetization, especially with ether, of a man who already has a wounded lung is of course most reprehensible.

The occurrence of jaundice may also lead to diagnostic difficulty. It may be due to hepatic injury, but it may also—at times appearing with great intensity and rapidity—be due to gas bacillus infection of the pleura when no subdiaphragmatic injury has occurred.

X-ray Examination. An *x*-ray examination of every case is essential to determine the presence, size, shape, and location of the missile. It is also useful as a means of corroboration of one's physical diagnosis. Mediastinal displacement, pulmonary collapse, free air or blood in the pleural cavity are readily demonstrable, and at times a pus collection can be located which would otherwise be sought for in vain. Short exposures and stereoscopic plates are very necessary.

The Uninjured Side. It is often more important carefully to determine the condition of the sound than of the injured lung. Upon the functioning of the uninjured lung the patient's life, at least for a time, almost entirely depends. The frequency with which signs of consolidation—which disappear after aspiration—are met with has been alluded to. One should always ask oneself: "How many lobes are functioning?"

It is remarkable in how many different directions and from what variable angles a lung may be traversed by a rifle or machine-gun bullet without doing any permanent damage. Small lodged shell fragments may be almost equally innocuous, but in the latter instance the danger of subsequent infection is much greater. In all cases, careful and prolonged observation and the avoidance of meddlesome surgery should be the keynotes of treatment.

THE PERITONEAL SYNDROME IN MALARIA

By H. C. Parsons, Lt. Col. C.A.M.C., Toronto, Ont.

THIS is the term applied by recent writers to the acute abdominal symptoms arising in the course of malaria. The picture of an acute abdominal accident is so clearly drawn that cases have been admitted to hospital as surgical emergencies, with diagnosis of appendicitis, intestinal perforation, gall stones, perforation of gastric ulcer, pyosalpinx, and even ruptured ectopic gestation. Laveran referred to it as "Malaria with symptoms of peritonitis," and speaks of the vomiting, severe abdominal pain, and distension. The literature of this condition is very scant. I am able to find only four references with dates from 1900 to 1905. The most recent treatise, that by Armand-Delille, Abrami, Paisseau, and Lemaire on the "Malaria in Macedonia," observations made during the period of occupation by the Allied armies, gives it only a brief note. I find no reference to it in the Johns Hopkins Hospital Reports 1895 (Thayer and Hewitson), nor in Thayer's "Lectures on Malaria," 1897, and I do not recall an instance while at Johns Hopkins Hospital, when it was my privilege to act as house physician to Professor Osler.

The malaria which we saw in Macedonia from 1915 to 1917 was unusual both in extent and severity; the clinical manifestations were most varied, and the syndromes corresponded to every system, cardio-vascular, respiratory, nervous, genito-urinary, ocular, gastro-intestinal, peritoneal, and the organs of internal secretion.

It is the peritoneal syndrome to which I would draw attention.

Pain in the abdomen was an almost constant complaint of soldiers admitted to hospital suffering from malaria. Vomiting, pain in the head, stomach, back, and legs was the usual formula, varying from a dragging sensation to acute pain. It was first felt in the left hypochondrium, and was found to be associated with an enlarged and tender spleen; at times there was a noticeable muscle spasm in this region. In the majority of cases this was a transient affair.

In more marked cases there was an extension toward the middle line, the upper abdominal zone being the seat of pain, tenderness, and rigidity.

In the still more marked form there was general abdominal pain, the whole abdomen was tender on pressure, there was some distension, and the muscle spasm was most striking. In some instances these signs were distinctly localized, the right side showing marked rigidity as compared with the left, and in several cases the right iliac fossa was rigid while the rest of the abdomen was soft, the picture of an acute appendix; or the upper right quadrant might be involved, simulating an acute gall-bladder infection.

The following cases quoted from the literature will illustrate these points: Gillot (1) cites the case of a woman admitted to hospital at Algiers in a typhoid state, supposedly enteric fever. She remained in this condition for several days, when acute abdominal symptoms suddenly appeared. Intestinal perforation was suspected and laparotomy was performed. Nothing abnormal was found, no typhoid lesions, no perforation; it was later found to be a case of malaria.

He reports two other cases of malaria with acute abdominal symptoms, one with marked localization in the right iliac fossa.

Soulié relates the case of a male forty-four years of age, with fever and rose spots, acute abdominal symptoms developed. Operation was advised, but the finding of the benign tertian organism in the blood revealed the true nature of the case.

In these reports no mention is made of the leucocyte count.

Jackson (2) reports these cases:

(1) Fever, chills, and sweating, with pain, at first in the upper abdominal zone, and later in the lower. The spleen was enlarged. The malarial parasite was found, leucocytes 8900 per c.mm.

(2) Diagnosis of pelvic peritonitis, with pain, tenderness, and resistance in the right iliac fossa. The spleen was enlarged. The malarial parasites were found, leucocytes 5100 per c.mm.

(3) A case with repeated attacks of malaria and acute epigastric pain with each recurrence. After the subsidence of the fever marked epigastric tenderness persisted for some days.

Capps (3) reports the following:

(1) Diagnosis of acute salpingitis. Chills and fever, to 103° daily.

The spleen was palpable. There was acute abdominal pain mostly in the lower zone. Leucocytes 5800.

(2) For six days patient had fever, headache, vomiting, and pain in the epigastrium so acute as to require morphia; admitted to hospital as a surgical emergency with a provisional diagnosis of gall stones, or perforating gastric ulcer. The spleen was palpable. Leucocytes 8900; this was considered evidence against peritonitis. Malaria parasites were found.

(3) Female, with a history of former pelvic trouble, chills and fever, but no pain at first. Later cramplike pain in abdomen and later localized pain right iliac fossa, so severe that she fainted. Spleen palpable, abdomen tender and resistant over right iliac fossa. Pelvis showed lacerated cervix and mass in left ovarian region, *not* tender. Extra-uterine pregnancy diagnosed, and brought to hospital for immediate operation. W.B.C. 5000. The benign tertian parasites were found.

(4) Diagnosis Appendicitis. Diarrhœa and cramplike pains in lower abdominal region on left side, vomiting. Subsequently with a chill, there was severe abdominal pain localised in right iliac fossa. Pain less between chills but renewed with them. W.B.C. 3000. Malarial parasites found.

The following cases will picture the condition as we saw it.

Case I. Private H., age twenty-five, was admitted to No. 4 Canadian General Hospital at Salonica on July 10, 1916, with a tentative diagnosis of malaria. On examination the spleen was found to be enlarged and tender and there was marked tenderness in the left hypochondrium.

July 12th. Patient complains of acute abdominal pain; this is generalised. There is marked rigidity over the entire abdomen, also great tenderness; there is no distension. Leucocyte count 8800 per c.mm.

Twelve hours later leucocytes are 18,000, the pain and rigidity persist more or less generally, but more marked in right iliac fossa. In view of this localisation of signs, and the rapid rise in the leucocyte count, the abdomen was opened. Nothing abnormal was found. The appendix was free from disease and the appearance of the peritoneum was normal.

The day after the operation the patient had a chill, temperature rising to 104°. The following day another chill with temperature of 103°. Blood examination showed the benign tertian parasite. Under quinine recovery was rapid and complete.

Case II. Cpl. B., age twenty-four. Malaria. The onset was two weeks ago, with severe headache, vomiting, chills, sweats, and general weakness. He had had no preventive quinine. Reported sick at Kukush, July 21, 1916. Admitted to 28 C.C.S. with temperature of 104.6° and was given quinine.

July 25th. On admission to No. 4 Canadian General Hospital the

temperature was normal, herpes on lips, tongue clean and moist, heart and lungs clear, spleen soft and palpable, abdomen slightly rigid. Tertian parasite in the blood.

July 31st. Has a severe diarrhœa, temperature 101°, pulse rapid, stools negative for dysentery group.

August 2d. Diarrhœa ceased, temperature 99°, pulse 98, markedly dicrotic. Patient complains of pain in epigastrium and left hypochondrium, abdominal respiration somewhat restricted, no distension; there is general rigidity, both recti very firm, the right more than the left, the hypogastrium very rigid and boardlike but resonant on percussion, spleen still palpable and very tender. Leucocytes 12,000.

August 3d. Leucocytes 14,000.

The abdominal signs and leucocytosis of 14,000 persisted for seven days.

August 13th. Tenderness and rigidity gone.

Case III. Private Hg. Admitted to No. 4 Canadian General Hospital, September 12, 1916. Diagnosis malaria. Benign tertian parasite found in the blood. Temperature 103°. He complains of pain in abdomen; on examination there is marked tenderness and rigidity and some distension. Enlargement of the spleen is doubtful. Leucocytes 7000.

September 13th. Symptoms and signs as before, leucocytes 14,000.

The leucocytosis persisted until September 16th. Pain and rigidity lasted until September 20th.

Case IV. Driver H., age thirty. Diagnosis malaria, second attack. Patient had been in the Struma Valley seven weeks, and had been taking preventive quinine. First attack in July. He was in the 28th General Hospital three weeks and returned to duty August 11th.

Reported sick September 16th, with "pain in head, back, legs and stomach." Chills and fever, diarrhœa, no vomiting. September 22d, admitted to No. 4 Canadian General Hospital. Temperature 103°. General condition fairly good, tongue furred. Heart, soft systolic bruit at apex, transmitted a short distance to the left. Apex is within mammary line. Lungs, coarse, dry râles over left side. Abdomen, full, tense, and tender, some rigidity, more so on the right side. Spleen easily felt and very tender. He is taking quinine, 40 grains daily.

September 23d. Temperature normal, abdominal pain severe, general tenderness and rigidity, more in the upper zone, but to less extent in the lower. Leucocytes 13,000.

September 25th. Distension marked, rigidity general, tenderness more marked over splenic region. This condition persisted until the 29th.

In this case the malarial organism was not found. The difficulty of demonstrating it in a case where quinine has been taken for a long period

of time is well known. There is no doubt as to the nature of the case from history and clinical findings.

CASE V. Private McC., age forty-seven. Diagnosis malaria (benign tertian). Patient had been on the Struma front for six months, and had taken quinine regularly. This is the first attack of malaria. He reported sick December 14, 1916, with pain in left side, headache, "shivers," fever, vomiting, and shortness of breath.

December 17th, admitted to No. 4 Canadian General Hospital. On examination, general condition fair, temperature 98°, tongue clear, heart and lungs clear. Complains of acute pain in lower left axilla. There is great tenderness over left side of abdomen and splenic area, and rigidity of the left rectus muscle, spleen enlarged, palpable, and tender. The benign tertian parasite is found.

December 19th. Marked rigidity of left side of abdomen, more so in the upper part and extending across the epigastrium to the middle line. Left rectus much firmer than right. On deep inspiration spleen is palpable and very tender. There is no cough; left side of chest clear; no signs of pleurisy.

December 22d. There is still a little rigidity in the upper left quadrant of the abdomen. Spleen still palpable. Left side of chest clear. No report of leucocyte count in this case.

It will be noted that while the abdominal signs in these cases were in the first place generalised, there was later a localisation which gave rise to a striking mimicry of a local condition.

Regarding the leucocytosis Jackson and Capps state that it does not occur, and hold that its absence is a point of differentiation from peritonitis. In this I cannot agree. The four cases in this series in which the count was made all showed a leucocytosis, it moreover was of the inflammatory type, with a relative increase or the polynuclear elements.

Again its appearance was sudden and corresponded to the increase in the acuteness of the clinical signs; in Case I, in twelve hours; and in Case III, in twenty-four hours.

This is precisely what happens in a perforation of an intestine, or a rupture of an appendix. It would appear, then, that the presence or absence of a leucocytosis has not the value that has been accorded to it for the purposes of differentiation.

The two points of real value are the presence of an enlarged spleen and the malarial parasite in the blood smear.

In Case I the indications for surgical interference were clear.

The definite localising signs, and the rapid rise in the leucocyte count from 8800 to 18,000 in twelve hours, left no doubt in the mind of anybody as to the urgency of the case, even though the existence of malaria was suspected. In Cases II and III the same question arose and the Medical Consultant advised operation until the facts of Case I had been related to him.

Causation of the Syndrome. It is evidently not from the effort and strain of vomiting. Capps states that it arises from coexistent disease or from neuralgia of malarial origin, or both.

When one considers the frequency of acute spleen tumor and perisplenitis in malaria, and the close relation of the convex surface of the spleen with the diaphragm, I think there is a more rational explanation. Clinically the pain and tenderness in the left hypochondrium appear to be the starting point. A tender spleen is almost the rule.

To explain the symptoms by an extension of the perisplenitis to the diaphragm appears reasonable. The abdominal symptoms that arise in the course of diaphragmatic pleurisy present a striking parallel. We have all seen such cases diagnosed as acute abdominal conditions, and some of them operated upon.

In diaphragmatic pleurisy and empyema—the diaphragm is extensively involved in the inflammatory change; this has been proved post-mortem. Whether it be the lesion of the diaphragm itself that gives rise to the syndrome directly, or indirectly through some nervous connexion or reflex, the mechanism of which we do not as yet understand, cannot be said, but the involvement of the diaphragm appears to be the origin of the trouble. The claim that these changes are of an inflammatory nature is supported by the appearance of a leucocytosis. In the milder cases this is not so apparent, but in the more severe forms, such as those under consideration, there is a change sufficiently great to express itself by changes in the blood.

BIBLIOGRAPHY

1. *Semaine méd.*, Paris, 1905, XXV, 433–5.
2. *Boston M. & S. J.*, 1902, CXLVI, 642–3.
3. *J. Am. M. Ass.*, Chicago, 1900, XXXV, 287.

STUDIES ON THE POTENCY OF DIGITALIS LEAVES FROM VARIOUS SOURCES

WITH COMPARATIVE TESTS OF THE ACTIVITY OF THE ALCOHOL-SOLUBLE AND THE WATER-SOLUBLE GLUCOSIDES

By Joseph H. Pratt, M.D., Boston, Mass.

STUDIES on the activity of digitalis were begun in the laboratory of the Department of Medicine of the Harvard Medical School in 1909, and have been continued to the present time by my associates and myself. I was led to undertake this work by the failure to obtain either therapeutical or physiological effects from digitalis obtained from the local druggists and at the Massachusetts General Hospital when employed in the ordinary dosage. Even in auricular fibrillation I never produced the characteristic slowing of the pulse until I used a digitalis leaf put up by Merck and imported from Germany by a pharmacist, at my request.

On December 1, 1905, I gave this powdered leaf as soon as it was received to a middle-aged woman who had cardio-sclerosis, auricular fibrillation, and marked cardiac insufficiency. She had been under my observation for more than a year. The chief symptoms were dyspnea, a troublesome cough, edema, and a scanty output of urine. A tenth of a gram of the powdered leaf was given three times a day. On December 8, a week later, I saw her again and made the following note: "The new digitalis has helped her greatly. The cough is much less, the pulse is slow but irregular and varies from 16 to 20 to the quarter. The rate at the apex is the same as at the wrist. To-day is the first time in six months I have found the pulse below 120."

As clinical tests made from time to time strengthened my belief that nearly all of the digitalis on sale in Boston was of poor quality, I tested in 1909 eight specimens of digitalis leaf by the thirty-minute frog method as recommended by Gottlieb (1) and Fraenkel. (2) A 10 per cent infusion was prepared and the minimum amount of digitalis required to produce systolic standstill of the heart determined.

The species of frog used in this and later work was *Rana pipiens*. The results are given in the following table:

TABLE I

10 PER CENT INFUSION. THIRTY-MINUTE METHOD. TESTS MADE DECEMBER, 1909

Mils of Digitalis Infusion per Gram of Frog Weight Required to Produce Systolic Standstill of Heart

Cæsar & Loretz, Halle, Germany, "titrated leaf V=5"	.014
Merck's German leaf	.020
Parke, Davis & Co.—German leaf	.035
Allen's English leaf. Sample A	.040
Squibb's German leaf	.040
Allen's English leaf. Sample B	.050
Allen's English leaf. Sample C	.050
Shakers of Ayer, Massachusetts leaf	.050
Squibb's German leaf. Sample B	.050

The strongest leaf was one I had obtained directly from Germany to compare with the digitalis sold in this country. The second in strength was obtainable only from the druggist who imported it. The biological analyses of the other specimens show that they were all of poor quality, in fact four were so weak in active principles that the characteristic digitalis action on the heart was not obtained even when large amounts were given. (3)

A year later Wesselhoeft and I tested seven lots of digitalis leaf. Instead of the thirty-minute method we employed a time limit of one hour, as originally suggested by Cushny, and first used by Famulener and Lyons (4) and later by Edmunds and Hale (5) in their important studies. A 10 per cent infusion was used in our tests, while Edmunds and Hale and other American investigators employed a tincture. The Cæsar & Loretz titrated leaf V = 5, and the Parke, Davis & Co. leaf had been tested the previous year by the thirty-minute method.

TABLE II

10 PER CENT INFUSION OF DIGITALIS USED. ONE-HOUR FROG METHOD. TESTS MADE DECEMBER, 1910

Mils of Digitalis Infusion per Gram of Frog Weight Required to Produce Systolic Standstill of Heart

Merck's German leaf. Sample A	.007
Cæsar & Loretz titrated leaf V=5	.009
E. R. Squibb & Sons. German leaf. Sample C	.012
Parke, Davis & Co. German leaf	.017
E. R. Squibb & Sons. German leaf. Sample D	.022
Merck's German leaf. Sample B	.024
Allen's English leaf. Sample D	.027

This study brought out several interesting points. The strongest leaf was obtained from the Boston druggist, who had kept a supply of Merck's imported powdered leaf in stock since 1905. It had apparently yielded good results in the practice of many physicians and was held in high repute. It was, however, not of uniform strength, and one lot tested by Wesselhoeft was found to be weak. A sample of the German leaf imported and sold by Squibb obtained directly from this pharmaceutical firm was of good quality. A second specimen of digitalis put up by Squibb and purchased from a Boston pharmacist was much weaker. (Table II.)

In 1909 five different lots of Allen's English leaf had been tested and found to be weak. A sixth sample was obtained in December, 1910. The frog test showed it to be less active than the other specimens of digitalis tested at that time, as is shown in Table II. It had been assayed in England in December, 1909, and the lethal dose was then .00054 mg. per gram of frog weight, according to the statement on the container. Doubtless the alcoholic extract (tincture) had been used in the tests made in England, and the result showed a high toxicity of the leaf at that time. Be this as it may, the fact was established that the aqueous extract (infusion) prepared from six different lots of Allen's leaf contained a relatively small amount of the active principles of digitalis. At that time Allen's leaves had a high reputation in America. The infusion from these leaves was regarded as especially active. Hale, writing in 1911, said, "At the present time English leaves are considered to be the best." Theodore Janeway(6), in his excellent paper on "The Use and Abuse of Digitalis," published in 1908, recommended Allen's leaves and favored the use of the infusion. Either the stock of Allen's leaf that he used was much stronger than our specimens, or the digitalis generally dispensed in New York was of very poor quality.

Although our tables show that the most active digitalis leaves assayed were obtained from Germany and that none of the English leaves were of high activity, the conclusion cannot be drawn that the German-grown digitalis is better than English-grown digitalis. It should be noted that only three lots of German leaf were of high value; two of these were specially imported and the third received directly from E. R. Squibb & Sons. Four specimens of digitalis

from Germany yielded an aqueous extract (infusion) of low toxicity, and the remaining lot tested, which was of a fair strength, was put out by Parke, Davis & Co. for experimental study and was not purchased in the open market.

As Merck and Cæsar & Loretz furnished digitalis leaves of higher activity to American pharmacists than did the English house of Allen, it is not surprising that, in this section of the country at least, the German leaf in the five years before the war came to be held in higher favor than the English, and its use rapidly extended.

Edmunds (7) in 1907 examined three tinctures made from German leaves and three from English leaves. The German leaves gave values of .004, .009, and .0125 mil; the English values of .0055, .010, and .0145 mil per gram of frog weight. As the standard fixed later by the American Pharmacopœia was a minimum dose of .006 mil of tincture per gram frog weight required to produce systolic standstill, it is evident that only one lot of German and one of English leaves examined by Edmunds yielded tinctures of standard strength.

The results obtained by Edmunds is a further indication of the poor quality of digitalis used in America at the time our studies were begun. In 1908 the strongest tincture tested by Edmunds and Hale was only half the strength set by the Pharmacopœia, as .012 mil of this tincture per gram frog weight was the dose necessary to produce systolic standstill of the ventricle. Fluid extracts of digitalis from four different manufacturers (Hance Bros. & White; Parke, Davis & Co.; Nelson, Baker & Co.; and Sharp & Dohme) diluted to tincture strength, were less than one-third of the standard now adopted by the Pharmacopœia. The inexcusable practice of preparing so-called tinctures of digitalis from fluid extracts by diluting with alcohol was fostered by one at least of the largest pharmaceutical firms, and I found tinctures were thus prepared by the pharmacists of two of the best known American hospitals, and in general use in these institutions.

Although Hale found that a lot of Allen's English leaves yielded high assay values compared with his assays of tinctures from leaves of unknown origin, even the English leaves were not up to the present standard. He did not study the strength of the watery extract, which possibly was no stronger than in the specimens of Allen's

leaves studied in our laboratory. Tinctures made from two lots assayed by us yielded high values when previously tested in England.

Roth (8) examined in 1914 twelve fat-free tinctures of digitalis purchased in the open market that year. They were prepared by twelve of the largest pharmaceutical firms in the United States. Only two of the twelve tinctures equaled the standard fixed by the Pharmacopœia. On the containers of six of the samples the statement was printed that they had been physiologically assayed. All were more active, however, than the tinctures tested by Edmunds and Hale in 1908.

The titrated powdered leaf prepared by Cæsar & Loretz was supposed to be of uniform strength. It was standardized according to the method of Focke. (9) The claim was made that it would not lose strength. This was doubtless based on the adoption of Focke's procedure of rapid drying of the leaf at a temperature of 80° as soon as gathered. Focke maintained that if the leaves thus dried were stored in air-tight bottles, the loss in activity from year to year would be negligible. At first they put out a leaf with the value of 5 according to Focke's Formula: $V=\frac{p}{d\times t}$. In this formula V represents the potency of the preparation, which was determined by dividing the weight of the frog p by the amount of the 10 per cent infusion d, multiplied by the time t required for systolic standstill to occur. A time limit of not less than seven or more than twenty-five minutes was fixed. In 1903, when he published his method, he stated that a good leaf should have a value of 5. In 1908 Cæsar & Loretz reduced the strength of the standardized leaf to 4.

TABLE III

STANDARDIZED LEAF OF CÆSAR & LORETZ TESTED BY ONE-HOUR FROG METHOD. 10 PER CENT INFUSION

YEAR OF CROP	TESTED	MILS OF INFUSION PER GRAM FROG WEIGHT
1907 (or earlier) V=5.	December, 1909	·008
1910 · V=4.	November, 1915	·025
1912 V=4.	March, 1917	·023
1914 V=4.	November, 1915	·020
1915	November, 1916	·045

* Corrected value, .023 mil. Frogs used in test resistant to digitalis. The dose of ouabain required to produce systolic standstill was twice the standard amount.

Five samples of Cæsar & Loretz' titrated leaves have been tested with the results given in Table III. All were kept in the original

bottles tightly corked. Only the first lot was of high potency. There was a great difference between the activity of this leaf and the other lots, as it was more than twice the strength of any of these. The remaining four lots were all practically of the same potency.

It is thus seen that the German leaf that was supposed to be of the highest quality and prepared in a way to preserve its strength unimpaired was of rather low activity, at least so far as the water-soluble alkaloids were concerned, at the time our tests were made.

American Digitalis. Before the War the greater part of the supply of digitalis used in the United States came from Germany and Austria. The pharmocopœial variety of the plant, probably indigenous to central and southern Europe, escaped from cultivation and was growing wild in great abundance in California, Oregon, and Washington, and to some extent in West Virginia (10) (11), but this source of supply had been neglected.

In December, 1910, Wesselhoeft tested in our laboratory a tincture made from Rocky Mountain digitalis by E. R. Squibb & Sons nearly two years before (January, 1909) and found it to have a lethal dose of .008 mil per gram frog weight, while the tincture obtained at that time from the Massachusetts General Hospital made from imported leaves was less than one-half that strength when tested on the same lot of frogs. In 1911 Hale (12) published some assays of American digitalis leaves. He found that a lot grown in the Government drug garden at Arlington, Va., in 1907, and a second lot of the crop of 1910, as well as a lot gathered in Madison, Wis., in 1908, were all more active than selected English leaves, tested at the same time for comparison. The lethal dose of tincture per gram of frog weight for the Arlington leaf was .005 mil, for Wisconsin leaf .0055 mil, while for the English leaf it was .007 mil. He later tested garden-grown first-year leaves from Seattle, Wash., which assayed .006 mil, and second-year wild-growing leaves from the same source .0085 mil. As the standard established by the U. S. Pharmacopœia IX is 0.006 mil of the tincture of digitalis per gram of frog weight, it will be seen that all these American leaves except the second-year Washington leaf met or exceeded this required strength, but that the English leaf did not quite meet it.

Rowntree and Macht (13), using the cat method of Hatcher and Brody, found that digitalis from the drug garden of the University

of Wisconsin was more active than any of four lots of Allen's English leaves in use at that time at the Johns Hopkins Hospital and far stronger than an old stock of German leaf in the hospital pharmacy.

Roth (11) in 1917 published assays on eight lots of American digitalis. Four samples of wild leaf grown in Oregon were stronger than the pharmacopœial standard, as was cultivated Wisconsin digitalis of the harvest of 1916. One lot grown in Ohio (cultivated leaf) equaled the standard.

Morrison and I tested freshly prepared tinctures made from twenty-three lots of *Digitalis purpurea* grown in various parts of the United States during the past three years. The results are given in the following table:

TABLE IV

Activity of Digitalis Purpurea Grown in the United States. One-Hour Frog Method. 10 Per Cent Tincture Used for the Tests, which Were Made at a Temperature of 20° C.

Year of Harvest	Source of Leaf	Mils of Tincture per Gram of Frog Weight
1916	Hobart, Wash. Wild. First year	·003
1916	Balleston, Va. Cultivated.	·003
1916	University of Wisconsin. Cultivated.	·004
1915	University of Minnesota.	·005
1916	University of Nebraska. Cultivated.	·005
1916	Greenfield, Ind. Cultivated.	·006
	Washington, D. C. Cultivated.	·006
1916	Portland, Me.	·007
1916	University of Minnesota.	·007
1917	Balleston, Va.	·007
1915	University of Nebraska. First year.	·007
1917	Linton, Ore.	·007
1916	Hobart, Wash. Wild. Second year.	·008
1916	Glenolden, Pa.	·008
1916	University of Nebraska.	·008
1917	Linton, Ore.	·010
1917	Washington.	·011
1918	Oregon.	·011
1916	Andover, Mass.	·011
1917	Linton, Ore.	·014
1916	Washington.	·014
1916	Seattle, Wash. Sample A.	·014
1916	Seattle, Wash. Sample B.	·016

Only seven of the twenty-three lots of digitalis leaves, that is, 30 per cent, yielded tinctures which equaled or exceeded the stand-

ard of the Pharmacopœia. The most active leaves came from the State of Washington and from Virginia, but it should be noted in this connection that the weakest three samples also came from Washington. There were five specimens of Oregon leaves, all of which were below the standard. As Roth assayed four lots of wild Oregon leaves and all were stronger than the Pharmacopœia required, it has been too generally assumed during the past two years that any Oregon wild leaf would be suitable for use in medicine. Large quantities have been gathered without preliminary assay and shipped to the eastern drug markets. One of our two most active samples was from first-year plants growing wild in Washington, the other was from cultivated plants growing in Virginia.

Some of the samples were air-dried. Digitalis received from the drug farms of the University of Wisconsin and the University of Minnesota were in air-tight containers. The digitalis from the University of Minnesota was prepared according to Newcomb's method, the leaf being dried in ovens at a temperature of 100° C. for eight-hour periods on three successive days.

Our study shows that highly active digitalis is grown in various parts of the United States, but a large proportion of the carefully collected samples of digitalis leaves, 70 per cent, was not as active as the Pharmacopœia demands. Probably the reason most of the digitalis on the market is of low activity is because a large proportion of digitalis is of poor quality when received by pharmaceutical firms. In the summer of 1918 we examined a well-mixed sample of a large lot of Oregon digitalis amounting to 830 pounds. Its activity was a little more than half the strength required by the Pharmacopœia. It is evident from these observations that samples should be assayed before the leaf is gathered in large quantity.

Preparation of Digitalis. It is held by most investigators of the subject that the leaves should be quickly dried by artificial heat as soon as gathered. Enzymes that break down the glucosides are rendered inactive by a high temperature. According to Focke (9) the leaves should be dried at a temperature not exceeding 80° within three days of gathering until the moisture content is reduced to 1.5 per cent. Hale (12) found that heat up to 120° could be applied for at least two hours to partially dried leaves, containing 10 per

cent moisture, without causing a loss of activity. Newcomb (10) believes that leaves should be dried at a temperature of 100° for eight hours on three successive days. This reduces the moisture to about 4 per cent. Roth (11) found that three specimens of Oregon leaf that had been dried in the air were of unusual strength. The most active sample assayed by him consisted of leaves that had partially dried on the stalk.

Whether the low activity of the Oregon leaves we have examined was due to lack of glucosides in the leaves, or to improper drying, cannot be stated. Although the method of drying is doubtless of importance, variation in the toxicity of new digitalis probably depends more on the amount of active glucosides contained in the fresh leaves. Digitalis obtained from the drug farm of the University of Minnesota was carefully dried under Professor Newcomb's supervision and was shipped in an air-tight container. The toxicity of the tincture was less than that of some samples that were not prepared with such care. The watery extract of the Minnesota leaf was strong, the minimum lethal dose being .007 mil. It is quite probable that rapid drying at a temperature of 100° C. preserves the active principles that are soluble in water better than methods in which less heat is employed.

Relation of Moisture Content to Deterioration. It is generally held that the more moisture left in the leaves the more rapid the deterioration. Focke holds that the moisture content should be reduced to 1.5 per cent within three days after gathering. The leaf is hydroscopic, but if moisture is taken up later, he claims little loss of strength may result. All samples of digitalis tested by Wesselhoeft and myself contained much more than 1.5 per cent of moisture.

A study of Table V shows there was no relation between the percentage of moisture and the activity of leaf as tested on frogs with a 10 per cent aqueous extract. Hale, using tinctures, was likewise unable to find any parallelism between moisture content of the leaves and the toxic value. Undoubtedly some of the moisture present had been absorbed by the leaves after drying. If the Cæsar & Loretz leaves had been dried according to Focke's instructions and preserved without the addition of moisture they would have contained only 1.5 per cent. It should be noted that the leaves from

the University of Minnesota dried at 100° contained more moisture than some of the other samples.

TABLE V

PERCENTAGE OF MOISTURE IN SAMPLE OF DIGITALIS AND MINIMUM LETHAL DOSE PER GRAMS OF FROG WEIGHT

	PER CENT MOISTURE	MILS OF 10 PER CENT INFUSION PER GRAM FROG WEIGHT
Cæsar & Loretz. Folia digitalis titrata V=5.	5·5	·008
Cæsar & Loretz. Folia digitalis titrata 1910, V=4. Newly opened bottle.	5·9	·015
Merck's powdered leaves. Old stock.	6·1	·024
E. R. Squibb & Sons' powdered leaves. Newly opened can.	6·3	·012
University of Minnesota. Newly opened can.	6·3	·007
Parke, Davis & Co. Powdered leaf.	7·6	·017
Hobart, Wash.	7·6	·008
Allen's English leaves. Old Stock.	7·8	·027
Glenolden, Pa.	8·7	·011
Merck's powdered leaf. Newly opened bottle.	9·1	·007

Deterioration of Digitalis Preparations. Comparative tests have been made over a series of eight years. Specimens of dried leaves retained their strength well. There was very little deterioration either of the alcohol-soluble or the water-soluble glucosides. It has been shown by a number of investigators that tinctures, as a rule, do not keep well. Symes, (14) in a careful study, found that deterioration may begin within a month from the time of manufacture, but one tincture examined by him and reputed to be twelve years old had an activity in excess of the standard. We tested two tinctures over a period of eight years; one, a tincture made from Rocky Mountain digitalis, which had a minimum lethal dose of .008 mil in 1910, required .021 mil in 1917. A tincture from the Cæsar & Loretz leaf, V=5, had an activity of .006 mil per gram when freshly prepared in January, 1910; in April, 1917, the lethal dose of this tincture was .021 mil. It is thus seen that more than three times the dose was required in 1917 than in 1910 to produce the same effect.

Comparative Tests of the Alcohol-soluble and the Water-soluble Glucosides. In a large number of specimens of digitalis obtained from various sources Morrison and I studied the relative toxicity of a 10 per cent alcoholic extract (tincture) and a 10 per cent infusion.

For years the infusion of digitalis has been held in high esteem by many clinicians, and it is possible that the water-soluble principles of the leaf are more important in therapeutics than those that add toxicity to the tincture but are not extracted by water.

Different lots of digitalis leaves vary widely in the relative amount of alcohol-soluble and water-soluble principles they contain as estimated by the biological test. Comparative tests of the toxic power of both the alcoholic extract and the aqueous extract were made on twenty-one different lots of digitalis leaves. The strongest 10 per cent alcoholic extract (tincture) had a value of .003 mil per gram of frog weight, the strongest aqueous extract .007 mil. The weakest alcoholic extract .016 mil, the weakest aqueous extract failed to produce systolic standstill of the heart when .045 mil per gram were given. Three samples of leaves yielded an extract with an activity of .008 mil. The alcoholic extracts from these three samples had values of .003, .005, and .006 mil. Leaves then of equal strength in water-soluble principles may vary 100 per cent in the activity of the alcohol-soluble principles.

The alcoholic extract was always found somewhat stronger than the aqueous extract, although the difference was slight in some specimens. The carefully dried leaf from the University of Minnesota gave values of .005 mil for the alcoholic extract and .007 mil for the aqueous extract. The Cæsar & Loretz titrated leaf $V=5$, which contained less moisture than any other specimen, and had been dried rapidly if Focke's directions had been followed, was found to have an activity of .006 mil for the alcoholic extract and .008 mil for the aqueous extract. Leaf from plants grown in Indiana from Oregon seed and from the Bureau of Plant Industry, Washington, D. C., likewise yielded values of .006 mil for the tincture and .008 mil for the 10 per cent infusion. From no other lots of digitalis leaves were alcoholic and aqueous extracts obtained that were so nearly of the same strength. As the University of Minnesota leaf and the Cæsar & Loretz digitalis were the two lots of leaves that were known to be dried at a high temperature soon after gathering, our results suggest that the aqueous-soluble glucosides were better preserved by the special methods of drying than by the methods of slow drying at lower temperatures which are in general use. We do not know how the Indiana leaves or those

furnished by the Bureau of Plant Industry were prepared, and the fact that the most rapidly dried leaves contained a large proportion of water-soluble glucosides may have been merely a coincidence.

There is evidence, as shown by Kraft,(15) that the most important water-soluble glucoside (digitaleïn or gitalin) is easily decomposed. It had long been held that the active glucosides in the presence of moisture change into substances that are inert or injurious. Some leaves containing 13 per cent of moisture were kept eight years in the laboratory and then alcoholic and aqueous extracts were prepared and tested. The former had a value of .009 mil per gram frog weight, while the latter required .026 mil per gram to produce systolic standstill.

Our study indicates that the toxicity of the aqueous extract is probably a better guide to the therapeutic value of a digitalis leaf than the alcoholic extract. At the present time the alcoholic extract (tincture) is used almost exclusively in the biological tests of digitalis by the frog method in America and England. The value of the aqueous extract of leaves used for the preparation of infusions should be biologically determined on frogs or cats, as many lots of digitalis were rated as fairly strong when the toxicity of the tincture was taken as the test, but which yielded infusions of low value.

The region where the digitalis grew seemed to influence the ratio of water-soluble to alcohol-soluble glucosides. Three specimens of digitalis cultivated in New England were all weak in the water-soluble glucosides, while tinctures prepared from two of them were fairly strong.

Digitalis stronger in water-soluble glucosides than the best obtainable titrated German leaf—that of Cæsar & Loretz—grows in the United States and can now be obtained and is available commercially. The water-soluble principles were assayed by the frog method, using a 10 per cent infusion in twenty specimens of American leaf collected from various sources. Fourteen of these were stronger in water-soluble glucosides than any lot of Cæsar & Loretz titrated leaf purchased since 1909. Selected and biologically tested Virginian leaf bought in the open market in the fall of 1918 had a value of .008 mil of 10 per cent infusion, while the strongest Cæsar & Loretz leaf V = 4 had a value of .020 mil. The tests showed that the American leaf was two and a half times as strong in water-

soluble glucosides as the best German digitalis that could be obtained before the war.

Summary. Most of the samples of digitalis imported from England and Germany before the war were below the standard now required by the American Pharmacopœia, and were too weak to produce physiological or therapeutic effects when given in the usual dosage.

Most of the digitalis collected from different parts of the United States during the past three years likewise failed to yield tinctures that were equal in strength to that demanded by the Pharmacopœia. Some of the digitalis grown in the United States, both wild and cultivated, has been found by biological tests to be as strong as any imported digitalis examined.

The alcohol-soluble and water-soluble glucosides vary in amount in different samples of digitalis. As the latter are probably more important in therapeutic activity, it would seem that the infusion should be used in the biological assay.

BIBLIOGRAPHY

1. Gottlieb, *München. med. Wchnschr.*, 1908, LV, 1265.
2. Fraenkel, *Ergebn. d. inn. Med. u. Kinderh.*, 1908, I, 88.
3. Pratt, *Boston M. & S. J.*, 1910, CLXIII, 279.
4. Famulener and Lyons, *Proc. Am. Pharm. Ass.*, 1902, L, 415.
5. Edmunds and Hale, *Hyg. Lab. Bull.* XLVIII, Wash., 1909.
6. Janeway, *Am. J. M. Sc.*, 1908, CXXXV, 781.
7. Edmunds, *J. Am. M. Ass.*, 1908, XLVIII, 1744.
8. Roth, *Hyg. Lab., Bull.* 102, Wash., 1916.
9. Focke, *Arch. d. Pharm.*, 1903, CCXLI, 128.
10. Newcomb, *Am. J. Pharm.*, 1912, LXXXIV, 201.
11. Roth, *Public Health Reports, U. S. Public Health Service*, Wash., 1917, 377.
12. Hale, *Hyg. Lab. Bull.* 74, Wash., 1911.
13. Rowntree and Macht, *J. Am. M. Ass.*, 1916, LXVI, 870.
14. Symes, *Brit. M. J.*, June 20, 1914.
15. Kraft, *Arch. d. Pharm.*, 1912, CCL, 118.

EPIDEMIC INFLUENZA IN CHILDREN

By John Ruhräh, M.D., Baltimore, Md.

THE epidemic of so-called influenza which prevailed in Baltimore in the winter of 1918 and 1919, and which affected children to a very considerable degree, presented a certain clinical picture not ordinarily met with in practice, and therefore merits a description.

In almost every instance in which the disease occurred in a household all the children exposed contracted it; occasionally one or more escaped. In the early part of the epidemic the disease was usually introduced into a household by one of the older members of the family, the children being affected generally within five days after exposure. All became ill on the same day or within a period of two or three days, so that in almost every dwelling in which the disease was introduced the entire family was in bed at the same time. Later in the epidemic instances were noted in which the adults escaped and the disease started in the children, although in some instances adults were subsequently affected. The disease was apparently transmitted by direct contact, but isolation in a household was rarely successful in preventing the spread to other members of the family, nor did masks seem to help in private residences. Whether this was due to the imperfect technic employed, or to infections through the mucous membranes of the eye, is not clear.

The clinical picture was striking, usually quite definite, and not like an ordinary cold. The child was almost invariably taken ill suddenly; sometimes the onset could be dated almost to the minute. In these cases the disease started with a vomiting attack or a slight chill, followed by high fever and marked prostration, but sometimes there were prodromes of an indefinite nature lasting for about twenty-four hours or less. The prostration was usually marked, the child was perfectly willing to be in bed, the face was flushed with a curious reddish-purple blush over both cheeks and sometimes over the entire face and neck, and this blush was sometimes very cyanotic, so as to produce a decided purplish tinge.

There was a marked conjunctivitis, usually, though not always, without much secretion, and occasionally there was noticeable photo-

phobia. Sometimes this was wanting, while in other cases it was so intense as to suggest that seen in meningitis. In a few children there was inflammation of the ocular conjunctivæ, which sometimes was limited to one eye.

In some cases there was a nasal discharge from the beginning of the disease, while in others this did not start until one to three days after the initial rise of temperature. In some instances the discharge was extremely profuse and irritated the skin about the nose, and in others there was comparatively little. In practically all there was a marked angina, the entire pharynx and tonsils and soft palate being intensely red and somewhat swollen. This inflammation extended over the hard palate and cheeks, but there was nothing which could be called a pathognomonic enanthem. Small punctate hemorrhages were not uncommon. This inflammation generally spread downward rapidly, in some involving the larynx, with production of hoarseness and croupy cough, and occasionally a laryngitis so severe as to require intubation. In others there was a tracheitis with considerable cough; while in most there was a bronchitis, frequently extending even to the finer bronchial tubes. This produced slight acceleration of breathing, and there was usually a great deal of irritable coughing. The amount of secretion varied, in some being very profuse, in others more or less limited. Occasionally there was a dry bronchitis with an extremely irritable cough, but apparently slight secretion.

Children were more or less exempt from the pneumonic complications so common in older people, but not entirely so. In infants under fifteen months of age broncho-pneumonia was not infrequently encountered, and presented no particular difference from that ordinarily seen, unless it was that most cases were of a rather severe type. In older children there was an occasional broncho-pneumonia or lobar pneumonia, and sometimes either an empyema or a serous exudate into the pleural cavity.

Otitis media and involvement of the mastoid were both comparatively infrequent, although owing to the large number of cases seen this complication was encountered often enough.

In most children the gastro-intestinal tract was not much disturbed apart from an occasional attack of vomiting, unless the child was forced to take food. In practically every instance where this was done an irritable condition of the stomach was produced which lasted for several days, during which time little or nothing could be retained. In a certain number of cases the other symptoms were mild, while there was very marked involvement of the gastro-intestinal tract, often with diarrhea and a ten-

dency to production of an acidosis. These generally recovered in two or three days if the stomach was not irritated by food or medication.

There was some albuminuria in cases with high fever, but the writer did not see any cases of nephritis due to influenza, with possibly one exception where the etiology was somewhat obscure.

The nervous symptoms were either a marked irritability, or, what was more common, a condition of drowsiness or stupor, sometimes almost amounting to coma, although the child could be easily aroused, but generally objecting to the interference and drifting off into slumber almost immediately. Occasionally there were mild symptoms of meningismus, consisting of slight retraction of the head, very marked headache, some dilatation of the pupils, with somewhat lessened reaction to light. In one child a marked influenza meningitis was observed.

The temperature presented several variations, all of which were frequently met with. In a large proportion of cases in patients under fifteen years of age the temperature was highest at the onset and gradually became lower and disappeared within three days. This led to the term "three-day fever." In other cases the temperature reached normal on the third day, remained normal one or two days, and then recurred for two or three more days, when the normal point was again reached. In either case the temperature was high for two or three days, then down in the morning to normal or below normal and very high in the evening, 104° to 105° or more, gradually returning to normal. In one or two instances this high irregular temperature persisted for ten days or more without any apparent complication. In almost every case in which the child was allowed to be up on the day following the fever, and particularly where any considerable physical exercise was indulged in, there was an immediate return of temperature and other symptoms which lasted from two to five or more days. After the second remission of temperature, when the normal point was again reached, any further rise was taken to mean some complicating inflammation. In many the high temperature was followed by two or three days of subnormal temperature.

The skin manifestations are important from the standpoint of diagnosis, although not pathognomonic. In addition to the purplish blush on the cheeks referred to above there was generally a diffuse redness and, in the severer cases, a diffuse congestion. This varied from time to time, but was present in almost all cases to a greater or less degree. The pressure of the stethoscope or of the hands left white areas which rather rapidly again became congested. In addition to this there were frequently small areas of an urticarial-like eruption. There was also in many an eruption resembling somewhat the rose spots seen in typhoid ever for the similar eruption seen in

colon bacillus infections. These varied in number and were usually most frequent on the chest, abdomen, and back, sometimes on the extremities and occasionally on the face. Once or twice they were so numerous as to lead to a lay diagnosis of measles.

Fatalities were uncommon, although where nursing was poor the cases with broncho-pneumonia very often died. Where proper care was given there were few mishaps except among children under two years of age. In addition to the deaths from broncho-pneumonia there were some very curious and intense infections. These patients were profoundly ill from the onset, markedly cyanosed, and more or less unconscious, with a high fever. There was much-disturbed heart action and irregular respiration, sometimes vomiting, and death supervened generally within forty-eight hours after the onset. These cases were unaffected by treatment, and the heart generally did not respond to stimulation, or if so, only for a transient period.

The diagnosis was comparatively easy in early life on account of the rather clear-cut symptomatology. The prognosis in children was good if one excepted the broncho-pneumonias, which were rather infrequent. The treatment was symptomatic.

AN UNUSUAL COMPLICATION OF MUMPS

By Joseph Sailer, M.D., Philadelphia, Pa.

THE seriousness of mumps as a disease when it occurs in epidemic form has never been justly estimated. In large groups the financial loss to the employer of the patients' time may be considerable. The disease is not dangerous to life. Rarely does it produce any sequel that impairs function; hence little attention has been paid to it from the standpoint of prophylaxis.

As nearly as can be determined the organism finds a culture medium upon which it can grow actively and produce its poisonous products, chiefly in the glandular tissues, salivary glands, pancreas, and testicles. Trousseau particularly has described the so-called cerebral mumps, a rare complication characterized by acute delirium or insanity, lasting usually twenty-four hours. I have seen one such case in Vichy Hospital Center in France following closely the description given by Trousseau. In this instance a spinal puncture was not done, and we have no knowledge regarding the reason that caused the cerebral disturbance. The rapid recovery from a condition of delirium, during which the man attempted to throw himself from the window of the ward, was the surprising feature.

During the winter of 1917–18, while I was in charge of the Medical Wards of the Base Hospital, Camp Wheeler, there was a brief epidemic of mumps among the soldiers in the camp that yielded about 6000 cases, the notable feature of which was the extraordinary rapidity of its spread. More than half of the cases developed within a period of two weeks, although there were several occasions before and afterward during which there were minor exacerbations.

Nothing could be learned about the mode of transmission. It seemed as if contact would hardly explain its extraordinarily rapid spread through the camp, nor as nearly as we could ascertain did it seem to start at one or more foci and gradually extend from them. Cases appeared almost simultaneously in all parts. There was

nothing that justified a suspicion of insect transmission. In fact at the time of the maximum incidence the camp was almost free of any form of biting insect, including fleas, lice, and bedbugs.

The features that impressed me most particularly were:

(1) The involvement of all the salivary glands. The parotid gland was most frequently and nearly always most conspicuously involved, but when sought the submaxillary and subinguinal glands were so frequently found swollen and tender that we concluded that mumps respects them almost as little as it does the parotids.

(2) The evidence of orchitis, which is a true metastatic manifestation, efforts to prevent infection through the urethra, and the administration of urotropin were equally ineffectual.

(3) The difficulty of proving conclusively that the abdominal symptoms were due to involvement of the pancreas. Various tests were employed, but none was positive. These symptoms were exceedingly frequent.

(4) The occurrence of a complication not hitherto described that I was led to believe indicated an involvement of the thymus gland. Altogether six cases of this syndrome were observed, $^{1}/_{10}$ of 1 per cent of all cases.

The general features of all of these cases were so similar that in spite of a slight variation in severity they may be described together. Usually on the third or fourth day of the disease, and sometimes later, swelling was observed over the manubrium of the sternum. This swelling was usually considerable, not sharply circumscribed. The tissue pitted on pressure and there was either no discoloration or very slight erythema, which often extended down the middle of the sternum and on either side as far as the midclavicular line, obliterating the supersternal notch.

Physical examination at this time showed dullness over the manubrium. The note became distinctly more resonant when the head was thrown back, the sign that is supposed to indicate enlargement of the thymic gland. There was no local tenderness, distinct dyspnea, not severe enough in any case to cause orthopnea, and there was no stridulous breathing on auscultation.

The *x*-ray was tried in all cases, and it was the opinion of Major Wheat, who took great pains to obtain profile exposures, that a shadow could be seen back of the manubrium, indicating enlargement of the thymus. The thyroid gland did not share in this enlargement.

During the persistence of the swelling there was a slight elevation of temperature, but the symptoms were not otherwise particularly severe. The edema was usually observed in slight form on the first day, reaching

its maximum the second or third day, and disappearing on the fourth or fifth day. As it subsided the dyspnea ceased and the patient returned to a normal state of health. There were no sequelæ. The change in note over the manubrium as the head was moved forward and backward ceased and a persistent resonant note was obtained.

The evidence that the thymus was involved may be regarded as suggestive but inadequate. Favorable are, first, the location of the edema; second, the alteration in the percussion note; third, the dyspnea, and fourth, the *x*-ray plates.

Against this is the absence of evidence that the ductless glands are ever involved in mumps. It is, however, possible that in the cerebral forms the pituitary gland is the seat of the active process. There is, however, no direct evidence that this is true. A very restricted access to the literature failed to reveal any record of such a complication, but in discussing the matter with others in the Medical Corps of the United States Army who had observed large epidemics of mumps, two similar observations were reported. At any rate it can be definitely said that in the course of mumps there occurs a presternal edema associated with slight dyspnea and yielding physical signs and *x*-ray pictures that suggest enlargement of the thymus, that this occurs in about one case in a thousand of mumps, and is probably not quite as rare as the so-called cerebral complication.

SEGMENTAL CEREBRAL MONOPLEGIA

By William G. Spiller, M.D.,

Professor of Neurology in the University of Pennsylvania

CORTICAL or subcortical monoplegia in which the paralysis is confined to a very limited portion of a limb is of rare occurrence, at least in civil practice. It is doubtful whether it could occur from a lesion as low as the inner capsule. The subject has attracted attention for years, but the observations have been comparatively few. A knowledge of this form of paralysis is important, because an incorrect diagnosis is probable when the patient is first seen, especially when there has been no injury of the head. A paralysis when confined in the upper limb to the shoulder muscles may be associated with weakness or even complete paralysis of the hip muscles or of all of those of the lower limb of the same side. When confined in the upper limb to the hand muscles it may be associated with partial or complete paralysis of the face of the cerebral type and with paralysis of the tongue, on the same side as the hand paralysis. The explanation of this association is to be found in the propinquity of the hip center to the shoulder center, and of the hand center to the face center. A cortical paralysis confined to the hand is very suggestive of peripheral nerve lesion, but impairment of stereognosis and of the senses of position and passive movement with preservation of other forms of sensation suggests the cerebral origin, and yet such sensory disturbances are not always present with paralysis from cerebral lesions.

Cases of paralysis of the shoulder muscles with paralysis of the lower limb of the same side are reported in literature. Bergmark, who was one of the first to write extensively on limited cortical monoplegia, refers to a case recorded by Oppenheim in which a tumor in the center for the leg gradually extended to the center for the arm, causing greater paralysis of the upper limb proximally; also to another case in which a cortical tumor caused greater paralysis of the hip and shoulder muscles. In Söderbergh's cases

with paralysis of the shoulder muscles there was also paralysis of the lower limb of the same side. The investigations of Holmes and Sargent on thrombosis of the superior longitudinal sinus have shown that the center for the shoulder muscles is the nearest of the centers for the upper limb to the centers for the lower limb, although the center for the trunk muscles intervenes. In the form of paralysis produced by a lesion of the superior longitudinal sinus and well studied by Holmes and Sargent, the finger movements either escape, or are weak for only a short time after an injury, and rapidly recover and regain their normal power. The hand movements never remain weak long except when the sinus lesion is complicated by an independent injury of the brain. The wrist movements, and especially those of the elbow, are affected more severely and recover less rapidly, while those of the shoulder often are disturbed when the more distal segments of the limb escape, and recover much less quickly when the whole limb has been implicated. The paralysis is pronounced in the lower limb, especially in the distal muscles, and may implicate all four limbs.

I have suggested that the easiest way to remember the distribution of the motor segments in the cortex is to consider these segments from above downward, as represented by an inverted man with the upper limbs extended beyond the head. We thus have the representation of the toes highest in the cortex, and then follow the centers for ankle, knee, hip, trunk, shoulder, elbow, wrist, fingers, and face.

The view that Bonhoeffer entertained, viz., that monoplegia affecting only the shoulder or the elbow with escape of the hand never occurs, is not tenable, as shown by Foerster, among others. Foerster described in 1909 isolated paralysis of the foot, of the interossei, and of the shoulder and upper arm with escape of the hand. Reich in 1913 could find no later work on this subject since the publication of Foerster's paper, and reported then several cases from Foerster's service in which the paralysis of cortical origin was confined to a small portion of a limb. A segmental representation of the limbs in the motor cortex, as accepted by Munk, is now established by clinical observation.

Söderbergh reported five cases of cortical or subcortical paralysis with greater implication of the proximal part of the limb. Either

there was complete loss of movement of the shoulder with intact finger movements, or weakness of the shoulder movements with intact finger and hand movements, or complete paralysis of shoulder movement with weakness of finger movements, or paralysis of the entire upper limb, except that there was flexion and extension at the elbow and hand with less finger involvement. Three of the cases were with brain tumor, determined by operation or necropsy, one was from sinus thrombosis caused by constriction of the superior longitudinal sinus, and one was from trauma of the uppermost part of the central convolutions. He was able to refer to seventeen cases in 1913 which showed the incorrectness of Bonhoeffer's contention. The infrequency of observation, he suggests, is probably because attention has not been directed to the subject.

Dejerine has seen cerebral monoplegia confined to the forearm and hand, and with Regnard has had a case in which the monoplegia consisted of Jacksonian attacks and astereognosis and paralysis limited to the thenar and hypothenar eminences and interosseous muscles. A tumor was found at the necropsy implicating the middle portion of the central convolutions. He refers to cases reported in which the monoplegia implicated only the toes and foot, states he has observed this type several times, and says a case of this character was reported by Ferry and Gauducheau. Dejerine regards the partial monoplegia as more frequent than the total monoplegia, and more frequent in the upper than in the lower limb.

The recent war has given more opportunity for observance of segmental cerebral monoplegia, which may assume a sensory as well as a motor type. Cestan, Descomps, Euzière, and Sauvage report cases in which convulsions occurred in a region of disturbed sensation of radicular type.

In the first case they report a lesion of the right parietal region resulting from the bursting of a shell, and the patient had convulsive movements which began in the left index and middle fingers and extended to the forearm and arm. The left hand was a little weak, and while the whole left upper limb showed impaired sensation, the impairment was chiefly marked along the radial side of the forearm and hand. Thus the convulsive movements in their commencement were in the pseudo-radicular region of disturbed sensation.

Their second case was similar. A lesion of the left parietal region, likewise caused by the bursting of a shell, gave rise to sensory epileptic attacks, consisting of paresthesia in the right upper limb, where objective disturbance of sensation was most pronounced in the inner side of this limb. In this case convulsive movements were absent.

The third case was one of lesion of the right parietal region, with convulsions beginning in the last two fingers of the left hand and disturbance of objective sensation predominating on the ulnar side of the hand and the external border of the foot. The fourth case was similar.

These cases do not prove that the lesion was in the motor area, producing irritation and convulsions, but they raise the interesting question whether lesions of the parietal lobe may cause reflexly convulsions beginning in the motor representation corresponding to the sensory; i.e., when the lesion causes a sensory disturbance of the hand may it reflexly cause irritation of the motor hand area. We have one of the best illustrations of the possibility of this in the facial spasms associated with trifacial neuralgia and produced in the distribution of the seventh nerve by irritation of the fifth nerve.

In the case reported by Parhon and Vasiliu a soldier was injured by a bullet in the left parietal region and the bullet did not enter the brain. As a result of this lesion a tremor like that of Parkinson's disease developed only in the right middle, ring, and little fingers, and all voluntary movement was lost in these fingers. Sensation in its various forms was diminished only in these three fingers. An operation revealed a fracture of the internal table of the skull, and the dura was not opened. Some voluntary power returned in the affected fingers after the operation. As the authors point out, the resemblance to ulnar palsy was striking. They refer to a case one of them had had, in which at the beginning of an apoplectic attack paralysis was confined to the thumb and index finger, was associated with clonic convulsions of the thumb and face, and was followed by brachial monoplegia.

The case reported above is employed by these authors to show how closely cortical paralysis may simulate peripheral nerve paralysis and how closely the motor center of a part is related to the sensory center of the same part; they do not suggest that these centers are identical, and in their case the limitation of the lesion could not be determined. This case and that of Dejerine and

Regnard are particularly interesting in connection with the first and second cases reported by me in this paper, in which the hand alone was affected at first. The weakness of the face in my second case was so slight it could have easily escaped detection. Important in this connection is the report of a case by Richter.

The case of paralysis of the right hand reported by him was one occurring during typhoid fever and was without necropsy. He remarks that the finer details of cortical motor localization have had rather unsatisfactory demonstration in human pathology, and refers to the three types of cortical monoplegia described by Oppenheim in his textbook: the crural monoplegia from lesion of the paracentral lobule and upper third of the anterior central convolution; the faciobrachial type from lesion of the middle portion of the same convolution; and the glossolabial type from lesion of the lower third of this convolution.

In Richter's patient paralysis of the right hand developed suddenly with paralysis of the right side of the face, headache, and complete loss of speech. He was said to have understood spoken and written words. Improvement began gradually after three weeks, especially in speech. When examined about one year after the onset the lower part of the right side of the face was weak. The right upper limb was moved voluntarily normally at the shoulder and elbow, although resistance in the muscles possibly was weakened. All voluntary movement was entirely lost in the right wrist and fingers. Electrical reactions of the hand were normal. Touch, pain, heat and cold sensations were diminished in the right hand, and these sensations became normal in the lower part of the forearm. Speech was slightly affected.

Richter believed that the lesion was either an embolism or hemorrhage affecting a small part of the motor cortex.

Marie and Lévy report a case of facial monoplegia following a shell wound of the head. At first paralysis of the upper limb was associated with the facial palsy, but the former lasted only eight days. The facial palsy was slight, but was of the upper neurone type. Marie and Foix have reported several similar cases, with or without anarthria and brachial paralysis. Careful observation of such a case ought to prevent any confusion with peripheral facial palsy, by the association with palsy of another part, perhaps of short duration, and by the type of the facial palsy.

Decidedly unique is the case of double monoplegia reported by Regnard, Mouzon, and Laffaille.

A woman, aged twenty-six years, had paralysis confined in the right upper limb to certain muscles of the hand and wrist. In the right lower limb certain muscles of the foot and leg below the knee were paralyzed, but flexion and extension of the leg at the knee and movements of the thigh were normal. The monoplegias were thus confined to the extremities of the two limbs. Cortical lesions were regarded as certain. The peripheral nerves could not be affected on account of exaggeration of tendon reflexes of the limbs, Babinski's sign, and absence of disturbance of sensation. A lesion of the spinal cord was improbable. The lesion was supposed to be syphilitic meningitis, causing disseminated plaques. In confirmation of this opinion were sixth nerve palsy and improvement under mercurial treatment.

No weakness of the face on the side of the weak hand was detected in my first case before the paralysis extended up the limb, and one might expect such weakness to occur, as several reported cases have shown that cortical anesthesia confined in the upper limb to the hand is associated with cortical anesthesia about the mouth on the same side, and slight weakness of the face and tongue was associated with the weakness of the hand in my second case. This close association in the cortex of the centers of sensation of the parts about the mouth and of the hand would suggest a similar close association of the centers of the motor innervation of these parts, and the case of Richter referred to above and my second and fourth cases are confirmative of this view.

In both cases reported by Gerstmann the disturbance of sensation was about the mouth and in the thumb and thenar eminence of the same side, and the lesion was in the opposite parietal lobe. These, and similar cases to which Gerstmann refers, permit the conclusion that the sensory center for the mouth must be very near the sensory center for the thumb. Another justifiable conclusion from this case is that pain and temperature sensations may be more disturbed from lesions of the parietal lobe than other forms of sensation, although parietal lobe lesions are more likely to disturb the senses of position, passive movement and spacing, and stereognosis.

A case similar to Gerstmann's is reported by Gamper, but it differs in that the anesthesia was on the ulnar side of the hand and

forearm, and in this respect resembling the case of Parhon and Vasiliu already cited, but the sensory disturbance of the face in association with the anesthesia on the ulnar side of the hand induced Gamper to conclude that two lesions occurred, as the centers affected were not adjoining.

In Popper's case a wound of the parietal lobe caused complete loss of all forms of sensation in all the fingers of the opposite hand, with less involvement of the thumb, but confined to the ends of the fingers.

Marie says he has been able to observe a certain number of brachial and crural monoplegias from head injuries during the war, and that the brachial form is more frequent than the crural. In the brachial monoplegias he has almost always found some signs of implication of the lower limb. He has observed motor and sensory paralysis confined to the hand quite frequently from injury of the Rolandic region and especially from injury of the middle portion of the ascending parietal convolution. He calls these palsies *mains corticales*. There is in these cases a weakness of the hand movement resembling slight lesion of the ulnar nerve and superficial and deep sensory disturbances of variable intensity in the different cases, and disturbance of stereognosis often pronounced and confined to the radial or ulnar part of the hand. He proposed to discuss these palsies more fully, but I have not found anything further than this brief statement from his pen.

The first case which I report is one in which a paralysis confined to the left hand was said by the patient to have developed rapidly and to have existed a little more than three weeks, and was chiefly in the ulnar and median nerve distributions. The man had been working overtime as a carpenter in the necessity that existed in preparing quarters for the drafted men. It was a period of great national stress. As sensory disturbance of a hysterical character was present at the first examination and disappeared rapidly under psychotherapy, it was thought at first that the paralysis of the hand might be hysterical, and under the treatment by psychotherapy and the stimulus thereby given to employ the motor power of the hand to the utmost the man seemed to gain power. He came to the dispensary several times, but the power of the hand never increased beyond the slight improvement produced at first. It became evident to me that the paralysis was organic, and as he had pressed the

left wrist with much force against the plane in long-continued labor it seemed possible that I might have to deal with a pressure palsy. On account of many patients coming to the dispensary and the difficulty of examining them properly with our depleted medical staff, the electrical examination was not made. It probably would have revealed no changes, as the paralysis was cerebral. The later development of the case permitted the diagnosis of tumor of the motor area of the brain, and operation was performed by Major C. H. Frazier with confirmation of this diagnosis.

In the second case the right hand alone was weak, the sense of position was greatly impaired, and stereognosis was lost in this hand. The muscles of the right corner of the mouth were a little weak and the tongue when almost fully protruded deviated a little to the right. Convulsions had begun in the right hand in the onset of symptoms and beginning papilledema was found. Dr. A. C. Wood, at my request, exposed the left motor parietal region, and a small tumor was found in the center for the upper limb, having the appearance of a tuberculous growth microscopically. A few small plaques were found in the parietal lobe.

The only indication of implication of the right lower limb was some exaggeration of the tendon reflexes of this limb, but Babinski's reflex was not obtained. As the fibers from the cortical center for the lower limb pass beneath the cortex of the center for the upper limb on their way to the inner capsule, it was evident that the lesion could not extend deeply into the brain, as otherwise there surely would have been a Babinski reflex and some weakness of the lower limb. The early Jacksonian convulsions also suggested that the lesion was cortical.

In the third case the possibility of hysteria also had to be considered. The patient had recently completed a beautiful home and had lost his wife about three months later. The first sign of weakness was detected during the funeral of his wife, when he stubbed the toes of his right foot in going upstairs. As he was an emotional man, the ground seemed well prepared for a hysterical attack. At my first examination, about three weeks after the beginning of his symptoms, there was slight right hemiparesis, which had developed very gradually with complete paralysis of the muscles of the right shoulder, while the grasp of the right hand was about as good as that of the left, although stereognosis and senses of position and passive movement were lost in the right hand. Within a few days the extension of the paralysis downward in the right upper limb indicated a cerebral lesion, and the further development of the case permitted the diagnosis of brain tumor. Operation was not desired by the patient or his relatives and a necropsy could not be obtained.

In the fourth case a paralysis of the right side of the tongue, of the

lower part of the right side of the face, and of the right hand, with indistinctness of speech, developed during sleep in a man thirty-seven of age. Movement at the right elbow and shoulder was normal. Much improvement occurred in the condition within three weeks. The lesion probably was in a small branch from the middle cerebral artery supplying the motor cortex affected.

I have no doubt many similar cases will be observed when attention is paid to the subject. Lack of space prevents the publishing of the notes of these cases in detail.

BIBLIOGRAPHY

Bergmark, "Review of Neurology and Psychiatry," 1910, 199.
Holmes and Sargent, *Brit. M. J.*, October 2, 1915, 493.
Spiller, *Progr. Med.*, September, 1916, 333.
Reich, *Deutsche Ztschr. f. Nervenh.*, 1913, XLVI, 446.
Söderbergh, *Deutsche Ztschr. f. Nervenh.*, XLIX, 253.
Dejerine, "Sémiologie des affections du système nerveux," 2d Ed., 255.
Cestan, Descomps, Euzière, and Sauvage, *Revue neurologique*, April and May, 1917, 235.
Parkon and Vasiliu, *Rev. neurol.*, April and May, 1917, 156.
Richter, *Neurologisches Centralblatt*, July 1, 1918, 450.
Marie and Lévy, *Rev. neurol.*, November and December, 1916, 513.
Marie, *Rev. neurol.*, November and December, 1916, 617.
Regnard, Mouzon, and Laffaille, *Rev. neurol.*, June 30, 1914, 838.
Gerstmann, *Neurol. Centralbl.*, July 1, 1918, 434.
Gamper, *Monatsschr. f. Psychiat. u. Neurol.*, January, 1918, 21.
Popper, *Neurol. Centralbl.*, July 1, 1918, 447.

THE RELATION OF THYROID SECRETION TO THE CONDITION OF THE SKIN—AND INCIDENTALLY TO OLD AGE

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As old age advances, the condition of the skin, nails, and hair undergoes certain changes. The skin becomes dry and scaly, is liable to wrinkle and crack, especially when exposed to cold air; and the normal secretion of sweat is diminished, even under the stimulus of exertion and of heat. The nails become ridged or striated, very hard, even horny, and very brittle. The hair loses its glossy appearance, is dry, breaks easily, and is liable to fall out, leaving the head bald.

These changes have been observed quite uniformly in patients suffering at any age from myxedema or milder states of hypothyroidism. It seems, therefore, as if the conclusion might be justified that in old age they are due to a lack of thyroid activity. Hence it has been my practice in recent years to prescribe small amounts of thyroid, not more than one grain of the Burroughs & Welcome extract, in divided doses, in a day, to all those persons above the age of fifty, who show any of these changes in the skin, nails, and hair.

It has been interesting to notice that in all cases under the use of thyroid these conditions of the skin, nails, and hair have promptly subsided, and have disappeared, not returning, unless the thyroid treatment is stopped. Incidentally it has been noticed that during such treatment the pulse tension, if at all abnormally high, has diminished, not infrequently from 15 to 20 mm.

It is not unusual for patients to mention, spontaneously, that they feel more active, mentally as well as physically, while taking thyroid. This is not surprising, in view of the well-known mental alertness of persons suffering from Graves' disease. It has been observed that it also tends to diminish depression and insomnia.

The conclusion, therefore, may be reached that some of the conditions supposedly due to old age are actually due to a diminution in the activity of the thyroid gland, and that consequently they may be obviated or removed by the constant use of thyroid extract as age advances.

RELATION OF ACUTE INFECTION TO DIABETES

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IT has been found by various authors that (I) acute infections with fever may occasion some disturbance of the carbohydrate tolerance with increase of blood-sugar and transient glycosuria; that in these circumstances, the administration of glucose is followed by excretion of sugar in varying, sometimes considerable, amounts (alimentary glycosuria); (II) that occasionally diabetes, temporary or permanent, may follow acute infections, and (III) that infectious diseases occurring in diabetic persons increase the disturbance of carbohydrate metabolism and precipitate other unfavorable conditions, notably acidosis; it has, however, been claimed by some writers that diabetes is favorably influenced by the intervention of an acute infection.

I. Though clinical observers had for a long time known that glycosuria occasionally appears in the course of infectious diseases, the direct demonstration that the carbohydrate tolerance is diminished and blood-sugar increased in febrile infections seems first to have been made by Poli, (1) who administered glucose in amounts of from 100 to 150 grams to patients who were suffering from scarlatina, diphtheria, septicemia, tonsillitis, and pneumonia, and found in many of them definite glycosuria. In two cases of pneumonia, the amount of sugar in the urine was 3 and 4 per cent respectively; and 7 and 8 per cent of the total ingested sugar was eliminated through the urine. Later Liefmann and Stern (2) reported the finding of marked increase in the amount of blood-sugar in febrile conditions (pneumonia) without any glycosuria. They made no attempts to repeat Poli's observations. Hollinger (3) also found high blood-sugar figures in cases of pneumonia and other febrile conditions. Tachau (4) also reported the finding of considerable hyperglycemia in febrile affections, and was able to increase the amount of blood-sugar notably, by the administration of sugar,

without precipitating glycosuria. Previous to these observations Roger and Bouchard (5) found that in experimental anthrax, after twenty-four or forty-eight hours, the blood of the animals contained from 0.224 to 0.297 per cent of sugar, while the serous fluids in the neighborhood of the injections were also heavily loaded with sugar.

It seems evident from these observations that a moderate or considerable hyperglycemia occurs in the course of various infections, and that the administration of sugar may produce alimentary glycosuria more readily than in normal individuals. These conditions are apparently frequent, though transient, in infections. How often they lead to more permanent results must be established from clinical observations in persons recovered from infections.

II. A complete review of the literature bearing upon the occurrence of glycosuria or diabetes during or after infections would not be especially profitable, because most of the publications date from periods when accurate clinical and chemical studies were not available. It will, however, be useful to refer to some of the readily accessible literature to show how frequently and in how many varied forms of infection sugar has been detected in the urine, though it will at the same time be noted that very few of the reported cases were followed to their conclusion. It is impossible to determine how often there was but an ephemeral or transient glycosuria, and how often an actual diabetes occurred. The emphasis laid upon the degree of glycosuria by older writers as determining the existence of actual diabetes seems without doubt to have been unwarranted. Severe diabetes may begin and perhaps continue without marked glycosuria, and, on the other hand, considerable amounts of sugar may be excreted in cases of mild diabetes, or possibly of transient glycosuria. It is not improbable that some and perhaps many of the cases of "glycosuria" met with during and after acute infections, if seen at intervals later, might later have turned out to be actual diabetes. Some such explanation is necessary to elucidate the fact that careful students of diabetes have so rarely been able to trace cases back to definite infections, if this origin is, indeed, a common one; and there seems good reason to believe that it may be, in view of the fact that certain observers have found undoubted instances and that disease of the pancreas is a complication that may readily occur in infectious diseases. Naunyn, Lepine, von

Noorden, Kleen, Allen, and Joslin refer to the probable etiological relationship, but say little of their personal observations, or while admitting the possibility, doubt the accuracy of many of the reports. Von Noorden (6) says, "In most of these cases the causal relation between the two diseases is very doubtful, furnishing an instance of the confusion of *post hoc* and *propter hoc*." After reciting a case in which diabetes seemed to have followed influenza, but was later found to have existed previously, he continues, "But it cannot be denied that acute infectious diseases may actually cause diabetes." Naunyn evidently accepted many of the older reports without expressing his conviction very clearly. Lepine is manifestly skeptical. Joslin (7) says: "The influence of infections has received considerable attention of late. In only a few instances have I been able to associate infectious diseases with diabetes; in fact, in only 28 cases of my series. When one considers the frequency of infectious diseases in a community and the rarity with which diabetes develops after the same, one is not inclined to assign great importance to infections." Further on he adds, "I certainly remain open minded on it." Though I am far from convinced that infection is the all-important factor, I am much impressed by the occasional striking cases that have come under my observation, and can readily believe that the connection may be difficult of demonstration because the development of the disease is frequently quite gradual. In this particular diabetes resembles arthritis, chronic anemia, and nephritis, conditions which are recognized as occurring insidiously after preceding infections or as a result of chronic focal infections.

I have purposely confined the scope of my discussion to acute infections; for this reason, in the references that follow, syphilis has been omitted, though much might be said on this subject. Naunyn refers to it extensively in his book.

Malaria. According to Kleen, (8) Peter Frank and Sydenham mentioned the association of diabetes with malaria (9). Burdel (10) makes a remarkable report showing the frequency of glycosuria in association with malaria. Among 134 quotidian fevers, glycosuria occurred in 25; among 122 tertian cases, in 17; among 78 quartan cases, in 11; among 40 of malarial cachexia, in 32; among 11 pernicious malarial fevers, in 3. The amount of sugar was small and usually below 0.5 per cent. His method of determination is not

mentioned. Verneuil (11) confirms Burdel's findings, and reports glycosuria in 17 of 110 cases of malaria without cachexia and in 76 of 100 cases with cachexia. Calmette (12) found sugar in 5 of 41 malarial soldiers, and Rumpf (13) in 13 of 100 cases of malaria.

These extraordinary figures have not been confirmed by others. Lepine (14) and Naunyn question the accuracy of the observations and, at all events, deny any relationship between such glycosuria and diabetes. Laveran (15) states that diabetes is rare where malaria is endemic, and Dieu (16) notes that diabetes is not more frequent in those parts of Algeria, where almost everybody has malarial infection, than in France.

Cholera. Heintz and Samjoe (17) first noted the occurrence of glycosuria in severe cases of cholera. Huppert (18) found that the sugar appeared as the patients began to recover and when the urine increased after the preliminary anuria. Neither he nor Gubler (19) saw the amount of sugar above 1 per cent. Usually the excretion of sugar is very transient, clearing up after two or three days. Naunyn states that the development of an actual diabetes mellitus has never been observed.

Diphtheria. Binet (20) found sugar in many severe cases of diphtheria, and Hibbard and Morrissey (21) also found transient glycosuria very common in severe and usually present in fatal cases. Occasionally it followed the antitoxin injection, and they considered it the result of the toxemia and not of the asphyxia accompanying the disease.

Mumps. Harris (22) reported a severe case of glycosuria following mumps, and assumed that the pancreas was affected. Garrod (23) also reports a series of cases of mumps with pancreatitis, in some of which glycosuria or transient diabetes occurred. Lepine, however, states that while a number of authors have reported instances of pancreatitis in association with mumps (24), diabetes was not found as a sequel, and he also mentions the fact that pancreatitis has been observed in typhoid fever without such a sequel.

Scarlatina, Measles, Pertussis, etc. In scarlatina, Zinn (25) and Stern (26); in measles, Stern (27), Barlow, Bordier, and others; and in whooping cough, Thomson (28) reported the occurrence of glycosuria in occasional cases. It has also been found in vaccinia, malignant pustule, variola, and in other infections.

Furunculosis and Minor Infections. The association of diabetes with furunculosis has been frequently discussed, and some of the observers thought that the glycosuria was the result of the infection. The leading authorities, however, unanimously regard the furuncular disease as the consequence of pre-existing diabetes, as this occurrence is very commonly observed in known diabetics. Somewhat the same view is held regarding other minor local infections—in the oral cavity, about the eyes, in the skin, etc.

Pneumonia. Rosenberger (29), Lion (30) and a number of other authors refer to glycosuria in this disease.

Influenza. Rumpf (31) found an apparently initial history of influenza in 15 cases among 100 diabetics. Holsti (32) and Kleen (33) also refer to cases.

The list of infectious diseases with which glycosuria has been found associated is by no means completed in the above tabulation. Occasional occurrences in other conditions, such as erysipelas, septicemia, hydrophobia, rheumatism, erythema nodosum, and gastro-intestinal infections, might be added.

It will be found from a review of this literature that so far as can be learned from the reports, the cases recorded have been with few exceptions instances of temporary glycosuria accompanying the infection named, and probably occurring only during the febrile period of the disease. In but a few of the reported cases has the history been followed, and the development of a lasting diabetes established.

In my own cases, to which I shall presently refer, the fact that, in association with or following acute infections, continuous glycosuria and more or less marked acidosis occurred, indicates that not merely a reduced carbohydrate tolerance, but actual diabetes, was developed. The possible occurrence of a pancreatic lesion as a result of the infection will be considered later.

The following cases, selected from my series of slightly over 200 cases of diabetes, though few in number, seemed striking enough to be placed on record. In each of them the patient was under observation long enough to determine that there was an actual diabetes and not a transient glycosuria. It is quite certain that none was diabetic before the occurrence of the infection which seemed to have precipitated or caused the diabetes. Probably 15 or

20 other cases might have been added had I included instances in which the history seemed to date from some acute infection, but in which the antecedent health of the patient was not certain.

CASE I. Severe diabetes following antrum infection and facial erysipelas; apparent complete recovery; 4½ years later, acute recurrence following influenza. Dr. W. W. S., aged twenty-four years, was admitted to the University Hospital March 7, 1914, with the evidences of severe diabetes. He had had measles in childhood, some digestive disturbance prior to appendectomy at thirteen years, and typhoid fever at seventeen. Later he suffered from repeated attacks of tonsillitis. On November 15, 1913, his tonsils were removed; November 22d, developed uveitis in his right eye, which continued for some time; December 2d, was seized with an acute febrile condition (grippe?) which was followed on December 10th by infection of the right antrum. From that date to December 17th, temperature ranged from 102⅖° to 105°; December 17th, developed facial erysipelas, temperature from December 17th to December 24th, 103⅖° to 106⅖°. December 25th, temperature fell to normal. He was profoundly prostrated after the attack. Early in January, 1914, slight increase in appetite, thirst, and urinary excretion were noted, but attributed to his recent illness and beginning convalescence. February 24th, sudden digestive disturbance and excessive polyuria—16,000 c.c. Distressing dryness of the mucous membranes and the polyuria led to urinary examination and the discovery of enormous glycosuria.

During his last two years as a medical student (1912 and 1913), he had been one of Prof. A. E. Taylor's "Food Squad," and had made daily examinations of his urine. Nothing abnormal was detected. During the acute illness (from November 27th to December 24th) he was under the care of my assistant, the late Dr. F. H. Klaer, who examined his urine several times. One complete record was preserved, which showed a specific gravity of 1.009, acid reaction, a trace of albumin, no sugar, no casts.

On admission (March 7, 1914) he was exceedingly emaciated (weight 123 pounds, normal 160 pounds), the skin and mucous membranes of the mouth were dry, there was a strong odor of acetone, perceptible even at a distance. On account of the evident acidosis the patient was kept upon a diet fairly liberal in carbohydrates and was given moderate amounts of alcohol. During this period the polyuria was pronounced, and the quantity of sugar and acetone bodies excreted were excessive. After five days the diet was considerably restricted, but some carbohydrate was allowed and the alcohol was continued. The amount of fat permitted was far in excess of what would be allowed at the present day. Despite this fact, the evi-

dences of acidosis diminished after a primary increase lasting a few days. There was at the same time a rapid falling off in the degree of glycosuria. The patient became sugar-free on April 14th, and the acidosis was reduced to negligible proportions soon afterward. The amount of blood-sugar remained distinctly higher than normal for some months after the disappearance of the glycosuria and ketonuria, but then fell to normal. During the time the patient was in the hospital his weight increased rather rapidly, and he had gained 14 pounds at the time when he became sugar-free. Subsequently the gain was more gradual up to the time of his recovery, which occurred several months later.

(At the time the patient came under observation, we were unfamiliar with Allen's methodical treatment, and practiced fasting only as a preliminary to von Noorden's oatmeal treatment when this seemed indicated. Had this case been treated by the methods of to-day, I have no doubt the glycosuria, as well as the acidosis, would have disappeared much more speedily.)

From April 14, 1914, until some time in December, 1918, the patient remained sugar-free. He gradually increased the amounts of carbohydrates in his diet, and except for restriction of sugar was using the diet of average normal persons. Late in 1914 he resumed medical practice, and during 1917 and 1918 was very active. In the fall and early winter of 1918 his work increased enormously on account of the influenza epidemic and war work in several industrial plants in which he was engaged as physician.

In December he himself fell a victim to influenza, the attack being fortunately mild; but immediately his glycosuria recurred and other symptoms (polyuria, emaciation) indicated a return of his previous condition. Readmitted to the hospital, December 10, 1918. There was little evidence of acidosis, but marked increase in the blood-sugar and decided glycosuria. Within forty-eight hours under a carbohydrate-free diet with moderate amounts of fat, the glycosuria disappeared, but the blood-sugar did not return to normal for one month.

Case II. Excessive glycosuria and severe polyuria occurring in the course of scarlet fever. No evidence of acidosis or other indications of severe diabetes. Glycosuria, however, obstinate. Death from meningitis. Miss E. A. S., aged twenty-five, a pupil nurse at the University Hospital, an exceptionally athletic young woman (champion swimmer, canoeist, etc.) had been in perfect health until the onset of a severe attack of scarlet fever which began about October 1, 1907. She was sent to the Municipal Hosiptal for isolation and treatment. While convalescent from the scarlatina, polyuria developed and glycosuria was discovered on October 16th. From this date until her discharge from the Municipal Hospital (November

29th) marked polyuria and glycosuria continued. Daily examinations showed quantities of urine ranging from 1200 c.c. to 3900 c.c.; specific

Diet	Amount Urine	Sp. Gr.	Glucose	Total N.	Ammonia N.	Ketones[1]	Plasma CO_2	Blood Sugar
3– 8–14 Liberal	9050 c.c.	1·031	576	—		42·9		
3– 9–14 Liberal	7600 c c.	1·033	512	—		39·3		
3–10–14 Liberal	7900 c.c.	1·030	445	—		39·4		
3–11–14 Liberal	7240 c.c.	1·033	457	—		38·2		
3–12–14 Restricted	4220 c.c.	1·030	140	—		45·9		
3–13–14	4020 c.c.	1·025	90.2	—		47·75		
3–26–14	2050 c.c.	1·029	61	—		—		
3–30–14	1630 c.c.	1·035	22	11·2		3·0		
4– 7–14	1450 c.c.	1·035	45	13·8		2·9		
4–14–14	950 c.c.	1·029	0	—		—		
4–27–14	830 c.c.	1·028	0	8·4		1·6		
6–11–14	—	—	0	8·6		1·8		0·118[2]
10–24–14	—	—	0	—		1·9		0·130
1–23–15	—	—	0	—		0·15		0·100
Re-admission 12–10–18 full diet	2160 c.c.	1·032	102·3	14·5	0·69	—	58%	0·26
12–12–13 carbo-hydrate-free diet.								
12–13–18 carbo-hydrate-free diet.	1270 c.c.	1·021	trace	—	—	—		
12–14–18 carbo-hydrate-free diet.	1770 c.c.	1·019	—	—				
1– 2–19 carbo-hydrate-free diet.	1800 c.c.	1·018	—	—	—	—		0·17
1–10–19 carbo-hydrate-free diet.	—	—	—	—				0·10

[1] Ketones are expressed in terms of acetone.
[2] Earlier records (much higher) have been lost.

gravities from 1.030 to 1.055; and sugar in amounts from 50 to 280 grams in the twenty-four hours. I received no report regarding diacetic acid, but

the fact that there was none after she came under my observation (November 30 et seq.) and that her physical condition did not in any way suggest the existence of an acidosis, leads me to believe there had been none prior to that time. During December, 1907, under strict dieting the sugar disappeared rather quickly, but it recurred very promptly after an attempt to increase the amount of carbohydrates. A second course of strict dieting again succeeded in rendering the urine sugar-free. A few weeks later the patient tried to resume her work as a pupil nurse (being then of necessity on a mixed diet), but the glycosuria promptly reappeared. During all of this time the patient appeared in the best of health as far as external appearance was concerned. Whatever loss of weight resulted from the scarlet fever had been regained before she came under my care and to all appearances she was in robust health. After a two weeks' trial it was evident that continuance of her nursing course was inadvisable, and the patient returned home to rest and strictly regulate her diet. Reports were sent to me at intervals, but I suspected that the glycosuria was only intermittently under control. In November, 1908, she returned to Philadelphia, and I found that the glycosuria was as pronounced as ever. Very shortly after this date she was persuaded to accept a minor position in a theatrical company, and I subsequently learned that she was taken acutely ill in Boston and died in February, 1909. Through the kindness of Dr. Joslin, some of the facts of her fatal illness were communicated to me by Dr. Hunter, who reported that Miss S. had been taken ill quite suddenly with sore throat and fever. When he saw her a few hours later the temperature was 99½° and the pulse rate 90; there was severe dyspnea and typical laryngismus stridulus. Subsequently she developed a stuporous and then an unconscious condition, with subnormal temperature and rising pulse rate. Finally, unequal pupils, retraction of the head, conjugate deviation of the eyes, and some spasticity of the muscles of the legs suggested the diagnosis of cerebrospinal meningitis. The patient died within thirty-six hours of the onset. A specimen of urine showed albumin and casts and an abundance of sugar, but no mention was made of diacetic acid or of any indications of acidosis.[1]

Case III. Mild diabetes following "grippe." Rapid disappearance of symptoms under treatment. Dr. J. C. C., age thirty-seven years, male, admitted to hospital on January 29, 1916. Dr. C. had felt perfectly well

[1] When this case came under my observation I was hopeful that the glycosuria would soon disappear under moderate dietetic restriction, in accordance with opinions then prevailing and reports available in the literature up to that date. After several trials and speedy return of the symptoms it became evident that there was more than a transient glycosuria, though the patient's general appearance did not indicate a severe form of diabetes.

until December 19, 1915, when he had a severe attack of "grippe." Two days later pain in left side, extending from the midclavicular line to the posterior axillary line at the level of the costal border; deep breathing or coughing aggravated the pain, which lasted about a week. His "grippe" continued until January 1st, and on January 6th he tried to resume his work, but found himself too weak to continue. From the beginning of his trouble he noticed great thirst and polyuria. Sugar was discovered in urine about January 20th. Examination of urine three months previously, as well as earlier examinations, did not show sugar. The patient's ordinary weight had been 145 pounds; on admission it was 130 pounds.

Physical examination showed no signs excepting enlargement of spleen. Various blood tests, including the estimation of the fragility of red cells, proportion of skein-cells, and morphological study of the red cells, negative. Duodenal contents showed the presence of the pancreatic ferments in apparently normal amounts, and a culture of the duodenal fluid showed the presence of a slightly hemolytic streptococcus, but two subsequent cultures failed to show this organism.

On admission, after two days of a carbohydrate-free diet, somewhat rich in fats, the urine showed 9.8 grams of glucose, 0.42 total ketones, 13.69 total nitrogen and 0.5 ammonium nitrogen, blood-sugar 0.19 per cent. He rapidly became sugar-free, and two weeks after treatment the blood-sugar was 0.09 per cent. Subsequently the patient was able to add carbohydrate to his diet, in gradually increasing amounts, without developing glycosuria, but under advice he avoided a rapid return to full diet and did not resume his medical work for a year. He has had no return of symptoms nor of glycosuria.

Case IV. Mild diabetes following vaccinia and infection of the arm. Readily controlled but relapsing on slight dietary indiscretions. T. H. D., age seventeen years, was admitted to the hospital on September 16, 1915. The patient was reported as having been perfectly well until he was vaccinated on December 3, 1914. He had a severe "take," and was in bed two days with chills and fever. The wound was infected and healed slowly. When the boy returned home on December 23d from boarding school, his mother noticed that he was thin and had an abnormal thirst and craving for food. The boy himself noticed three or four days previously that there was increased frequency of urination. The urine was examined by his family doctor and found to contain sugar. On admission to the hospital after a light diet for twenty-four hours, the urinary examination showed: amount 4950 c.c., glucose 369 grams, total nitrogen 14.53 grams, ammonium nitrogen 1.71 grams, total ketones 4.9 grams. Examination of the pancreatic secretions showed all the ferments present in normal amounts.

Schmidt's test showed normal pancreatic secretions in the intestinal tract. There was no abnormal amount of fat in the stools. On a carbohydrate-free diet, sugar rapidly diminished and in five days disappeared entirely. A little later he was troubled with an abscess at the root of one of his teeth, which seemed to be the occasion for the reappearance of sugar, but after careful dieting and relief of the abscess, sugar disappeared from the urine in three days. October 1st, urinary examination reads: amount 960 c.c., glucose negative, total nitrogen 8.45 grams, ammonium nitrogen 0.46 grams, total ketones 2.55 grams. The patient remained sugar-free with an occasional recurrence of sugar which was attributed to dietary slips. October 31st the urine report reads: amount 2015 c.c., glucose negative, total nitrogen 11.46 grams, ammonium nitrogen 0.73 gram, total ketones 0.87 gram. Subsequently, and until the time of his discharge, the patient remained sugar-free. He later had some recurrence of sugar, but always as the result of dietary indiscretion. A year later his father reported that he had had two remissions, probably attributable to dietary indiscretions, but each of these was readily controlled by more rigid dieting.

Case V. Moderately severe diabetes following pneumonia. A. G. W., age thirty-four years, male, admitted to hospital May 22, 1916, on account of frequent urination, polyuria, and increased thirst. Patient first noticed these symptoms and also increased hunger about the middle of February, 1916, immediately following an attack of pneumonia from which he was not yet convalescent. The symptoms began before he left his bed after the pneumonia. About March 1st sugar was discovered in his urine. The Wassermann was negative. The patient rapidly became sugar-free on a carbohydrate-free diet, rather rich in fats, but subsequently showed a tendency to recurrences of traces of sugar on a similar diet with very moderate additions of carbohydrate. At the time of his discharge in June he was sugar-free.

After discharge from the hospital, patient remained sugar-free for three months, when he was persuaded to increase his diet considerably, and the original symptoms recurred. During the next two years his condition is not recorded. He was readmitted to the hospital in July, 1918, with very much more pronounced evidences of diabetes. On a general diet, the twenty-four hour excretion of urine was 3700 c.c., specific gravity 1.038, glucose 290 grams, total nitrogen 17.47 grams, ammonium nitrogen 4.9 grams, total ketones 10.75 grams, plasma CO_2 36 volumes per cent, and the alveolar air CO_2 18. On August 25th the urine report reads: amount 1200 c.c., specific gravity 1.036, total nitrogen 9.72 grams, glucose 22.7 grams, ammonium nitrogen 3.14 grams, total ketones 7.34 grams. At the time of the patient's discharge from the hospital September 5,

1918, he was in much better condition, having been for some days sugar-free and free of diacetic acid reaction.

URINE.

Diet	Calories	Quant.	Sp. Gr.	Glucose	Total N.	Ketones	Bld. CO_2	Ammonia N.
5–23–16 House diet		3800 c.c.	1·045	258 g.				
5–24–16		710+ c.c.	1·042	22				
5–25–16		1165 c.c.	1·023	3·4				
5–26–16 Prot. 77.5 Fat 122.5	1452	1475 c.c.	1·021	faint trace				
5–27–16 C. H. 10.		1520 c.c.	1·025	faint trace				
5–28–16		1430 c.c.	—	0	14·3	0·4		0·63
Readmission 7–15–18, full diet		3700 c.c.	1·038	290	14·47	10·75	36%	4·9
7–19–18 Prot. 26.5 Fat 48.	514	1200 c.c.	1·036	22·7	9·72	7·34		3·4
7–20–18 C. H. 9.								
7–30–18, fasting		—	—	—	—	—		
8– 2–18		2000 c.c.		0				

In the foregoing cases, with the possible exception of Case III, the condition arising in the course of or immediately following an acute infection could be properly designated as diabetes, and in three there was a considerable tendency to acidosis. The statement usually made by writers on diabetes that "the carbohydrate tolerance is reduced by febrile infections" does not suffice, at least in the three cases with tendency to acidosis, to explain what took place. There were, in fact, all the metabolic phenomena of genuine diabetes, including the perverted fat metabolism with the resulting acid intoxication. The thought readily suggests itself that there may occur in the course of infectious diseases the pancreatic lesions that occasion diabetes. If this be the case, explanation must be given for the fact that diabetes so rarely occurs in cases of "acute pancreatitis," as this disease is ordinarily defined. In answer to this question, it may be pointed out that diabetes does not, as a rule, occur in various destructive lesions of the pancreas, such as carcinoma and chronic pancreatitis of biliary origin, and the acute pancreatitis commonly recognized clinically probably belongs to the same group of conditions, and is no doubt the result of irritations or infections ascending the pancreatic ducts from the duodenum,

whereas the lesions of the pancreas that occasion diabetes more likely have a hematogenous origin. Hematogenous infection of the pancreas, like involvement of other glands, is undoubtedly common in various infectious diseases; the occurrence of diabetes as a sequel of infection is, therefore, not improbable. As a matter of fact I have observed one fatal case of acute pancreatitis with rapidly developed diabetes and death in coma (to be reported later) and another case of severe diabetes originating in an acute pancreatitis of unknown etiology. It does not seem to me improbable in such marked instances as Case I, that the infection caused an acute lesion of the pancreas capable of producing the phenomena of diabetes, or that in other cases, and perhaps much more frequently than now appears probable from available evidence, pancreatic lesions initiated during infections eventually become sufficiently extensive to occasion diabetes.

III. Opinions regarding the effect of infectious diseases on an existing diabetes seem to have undergone considerable alteration. Older writers quite uniformly refer to the ameliorating influence of infections in a certain proportion of cases, while the attitude of contemporary authorities is to regard infections as uniformly unfavorable. Naunyn (34) says that "The reduction of glycosuria upon the incidence of acute febrile infections is simply astonishing," and elsewhere (35) he discusses the improvement in the diabetic condition during or following typhoid fever, pneumonia, relapsing fever, and other infections. While his statement gives the impression that this favorable effect of infections is usual, he mentions cases and published records that indicate the reverse, and in particular, refers to the fact that sometimes diabetic individuals temporarily sugar-free exhibit a return of glycosuria after the onset of an infection, giving the appearance of diabetes resulting from the infection. He makes special mention of the fact that glycosuria increases with the development of boils, carbuncles, or gangrene and greatly diminishes, or disappears, upon opening or drainage of the purulent collections or amputation of the gangrenous extremity. Von Noorden (36) says: "I have already had occasion to note the fact that in many cases of diabetes the urine becomes less saccharine or entirely sugar-free during the intercurrence of an acute pyretic infectious disease. This is an old experience. Typhoid fever and

relapsing fever are most commonly known as glycosuria-lessening; I have observed the same result in fibrinous pneumonia and influenza." On the other hand, like Naunyn, he believes that certain instances of apparent onset of diabetes during or after infections are really cases in which a latent (or temporarily aglycosuric) diabetes has been revived by the infectious disease. Lepine favors the view that infections are prone to aggravate diabetes, and, in particular, emphasizes the unfavorable effect of influenza. However, he quotes the case of Glaessner, (37) in which a severe diabetes with acidosis was apparently cured by an attack of pneumonia. Kleen (38) also refers to the favorable effect of infections in some cases, and contrary to Lepine, mentions distinct improvement after influenza. My own experience coincides entirely with that of Joslin: "Almost without exception intercurrent infections have increased the severity of an active diabetes, and in a large proportion of cases have been the immediate forerunners of coma." Several of my cases, in which the disease was either quiescent or clinically cured, at once relapsed upon the occurrence of an infection. This will be noted in the later history of one of the cases cited above as instances of diabetes originating from infection (Case I), and will be further illustrated in the following group. A very instructive instance showing the unfavorable influence of infections was that of a medical colleague who was the victim of the disease. During several years he had from time to time recurring attacks of acute sinus infection, after each of which there was a sharp increase in his diabetic symptoms and distinct evidences of acidosis. His final and fatal attack ending in coma was precipitated by the same cause.

The following cases illustrate the tendency of diabetes to relapse upon the occurrence of acute infections. In these cases there was less evidence that the original onset of the condition was attributable to infection, though the probability was considerable in Case VI.

Case VI. Diabetes probably following antrum infection. Recurrence and rapidly developed coma following facial erysipelas. F. M., age fifty years, negro, was admitted December 22, 1916, on account of an acute febrile illness which began two days previously. There was severe cough and some expectoration, considerable coryza, mucous nasal discharge, pain in the right side provoked by deep breathing and coughing. The patient also had severe frontal headache and tenderness over the right antrum.

Subsequently there was marked evidence of sinus trouble. On December 29th the left antrum was opened and found full of foul-smelling pus. There was also opacity of the left frontal sinus which required subsequent flushing.

The patient's previous medical history was of no definite significance in connection with the diabetic condition subsequently discovered. He had had some of the diseases of childhood and pneumonia on the right side four years previously; also malarial fever twenty-five years previously. There was no history of venereal infection. He was a married man with five healthy children living; was a chauffeur and, consequently, was considerably exposed to the weather. Family history negative.

The first examination of his urine after admission showed considerable sugar, acetone, and diacetic acid. A twenty-four hour collection, after a carbohydrate-free diet of about 2000 calories, was 750 c.c., specific gravity 1.032, glucose 8.25 grams; a second twenty-four hour collection was 900 c.c. and contained 14.5 grams of sugar. On both occasions a strong acetone reaction and a marked ferric chloride reaction were obtained. Complete chemical studies were not made. On a carbohydrate-free diet, the amount of sugar diminished to faint traces, and after four days of green diet, the sugar disappeared entirely.

Subsequent inquiries developed the fact that there had been no sugar in the patient's urine on any occasion previous to his acute illness. A number of examinations had been made on different occasions.

Readmission. Patient was readmitted to the hospital March 5, 1919. On March 2d an operation for the drainage of one of the accessory sinuses of the nose was done at another hospital, and the patient allowed to return to his home a few days later. He was admitted to the University Hospital on the above date with a well-developed facial erysipelas and marked fever, ranging from 104° to 105°. He stated that during the two years since his former admission to this hospital he had become careless regarding his diet and intermittently had suffered from polyuria, especially recently.

On admission, the urine examination (morning specimen) was reported as follows: specific gravity 1.022, acid, no albumin, *no sugar*, no casts.

As a precaution against possible acidosis the patient was put on a diet containing considerable carbohydrate in the form of oatmeal and other cereals and one-half ounce of whisky was given at third-hour intervals. March 16th: Twenty-four hours collection of urine showed *neither sugar nor ketone bodies*. March 17th: Blood urea N, 15 milligrams, plasma CO_2 46 volumes per cent, blood-sugar 0.18 per cent. March 18th: Urine, amount 1040 c.c., specific gravity 1.030, total nitrogen 8.82 grams, glucose 34.3 grams. Ammonium nitrogen 1.02 grams, total ketones 5.8 grams, a trace

of albumin, and many granular casts. March 19th: Blood urea N, 30 milligrams, blood-sugar 0.37 per cent, blood CO_2 22 volumes per cent.

On March 18th the patient grew more and more drowsy and died in coma on March 19th.

Case VII. Mild diabetes recurring acutely during an attack of influenza. A. H., age sixteen years, admitted to the hospital December 16, 1917. Had first experienced frequency of urination and marked thirst about 2½ months previously. Soon he began to lose weight and in all lost 14 pounds up to the time of admission. Appetite was enormous, but he was growing steadily weaker. Patient weighed on September 16th 123 pounds, and on December 17th, 103.

The patient's tonsils and adenoids had been removed four years before, but he had suffered from an attack of ulcerative sore throat five months before the onset of the present symptoms, and had practically not been well from then up to the time the present illness was observed. In November, 1917, the patient had been in another hospital, where the following analyses of the urine were reported: November 15th, sugar 31.25 grams per hundred c.c.; 19th, sugar 3.12 grams per hundred c.c.; 23d, sugar 0.25 gram per hundred c.c.; 26th, negative.

Between this date and admission to the University Hospital the glycosuria had reappeared.

On a carbohydrate-free diet he was quickly rendered sugar-free, and remained so during the two weeks that he was in the hospital, except on one day, when he excreted 7.2 grams of glucose, probably on account of a little intake of fruit.

From the date of discharge from the hospital, December 20, 1917, until January 19, 1919, the patient remained sugar-free with two exceptions, when during one day from excessive intake of fruit, traces of sugar were found. His diet ranged from 50 to 70 grams of protein, 100 to 120 grams of fat and from 40 to 80 grams of carbohydrate. He was engaged in light office work.

During December, 1918, he had a mild attack of influenza and immediately thereafter he experienced symptoms, and sugar reappeared in the urine in considerable quantity. He was at once put on a carbohydrate-free diet with considerable reduction in both fats and protein and became sugar-free in a few days. After two weeks rest from work, he was practically in the same condition as before the attack of influenza, and since then has gradually resumed a full diet low in fats, but with considerable addition of carbohydrate.

Case VIII. Severe (or prolonged) diabetes; apparent recovery under treatment; rapid recurrence and death in coma during an attack of in-

fluenza. F. H. M., age thirty years, male, admitted to hospital March 1, 1916, on account of severe diabetes. His physician stated that the patient's illness began about four years before without apparent cause. The patient first noticed thirst and marked fatigability; later he complained of gastrointestinal disorders and nervous depression. Sugar had been discovered almost at the beginning of the illness, and he was never sugar-free, though some attempts at strict dieting had been made. The patient was extremely emaciated, temples sunken, skin pallid, and a marked acetone odor was noticed in the room where he was sitting. No special physical signs. On a light diet, not restricted as to carbohydrates, the output of urine was 2850 c.c., specific gravity 1.039, glucose 150 grams and acetone and diacetic acid ++. Subsequently after three days' fasting he became sugar-free and remained so with rare exceptions, when traces of sugar reappeared. The diet was rather too high in fats, and, though sugar-free, the urine contained diacetic acid till shortly before the patient's discharge from the hospital (April 30, 1916).

	Amount	Sp. Gr.	Glucose	Total N.	Ammonia N.	Ketones
3– 9–16	1240 c.c.	1·040	30·3 gms.	11·1 gms.	2·77 gms.	8·89
3–30–16	1570 c.c.	1·015	negative	9·8 gm.	0·35 gm.	0·812

Weight on admission was 101 pounds, and at the time of discharge, 98 pounds. After discharge from the hospital, increasing amounts of carbohydrates were added to his diet. Weight and strength increased steadily. January 1, 1917, he weighed 113¼ pounds; subsequently remained stationary at about this point. Sugar never reappeared in the urine until his fatal illness.

On November 27, 1918, patient had symptoms of a mild attack of influenza, and was put to bed at once. He improved so much that his physician did not think it necessary to see him every day. He last visited him December 1, 1918, and found his patient in good condition. On December 2d the patient went into sudden coma, and death occurred during the night, December 3d.

Case IX. Mild, but prolonged, diabetes; rapid recurrence and death in coma during an attack of croupous pneumonia. Mrs. L. J. S., age sixty-six years, consulted me on March 12, 1918, on account of diabetes, which was recognized five years previously. In the beginning of her illness there was marked thirst and frequent urination. Under strict diet she had been relieved of these symptoms and the glycosuria, but had recurrences of sugar with any attempt at increasing her diet. At her first visit a sample of

urine showed a small quantity of sugar, but the twenty-four hour excretion was not determined. With restriction of her diet, the sugar promptly disappeared, and during the next six months was constantly absent in the twenty-four-hour collections. A slight return was noted on one occasion at this time, but thereafter she remained sugar-free for another six months. On February 15, 1919, after having been free of sugar for twelve months, she was seized with a severe attack of croupous pneumonia. Her physician found a large amount of sugar on the same day and when I saw her, twenty-four hours later, she was in a stuporous state with apparent diabetic acidosis. The urine contained 2.5 per cent sugar and showed a marked ferric chloride reaction for diacetic acid. She died a few hours later with increasing pulmonary engorgement and with pronounced coma.

Conclusions. The cases of diabetes here reported illustrate the occasional onset of this disease during or immediately following acute infections, and the marked tendency of infectious diseases to cause recurrence of diabetic conditions after the arrest or apparent cure of the disease. The recurrence of diabetic phenomena in two of the cases (Case I and Case VIII) after apparent cure of four and two years' duration respectively, immediately after the onset of acute infections, indicates the difficulty in determining whether or not the arrested disease is actually cured. The greater intensity of the disease when recurring after primary arrest (Case V, and less clearly Case VI) indicates the probability that many of the instances reported in literature as transient glycosuria in the course of infection might have later recurred as genuine diabetes, when the original infectious origin would not have been recognizable. Undoubtedly infection must be regarded as a probable cause of the pancreatic lesions that occasion diagnosis, and for which at present no established etiology is recognized. The evidence of such cases as are here reported is of course regarded merely as suggestive.

BIBLIOGRAPHY

1. *Festschr. des städtisch. Krankenhaus*, Frankfort, 1896.
2. *Biochem. Zeitschr.*, 1906, 299.
3. *Deutsches Arch. f. klin. Med.*, 1907–08, XCII, 217.
4. Ibid., 1911, CIV, 437.
5. Quoted by Naunyn, "Der Diabetes Melitus," 1898, 113.
6. "Twentieth Century Practice," II, 65.

7. "Treatment of Diabetes Mellitus," 2d Ed., 62.
8. "Diabetes Mellitus," P. Blakiston's Sons & Co., Philadelphia, 1900.
9. For literature, Kleen refers to Jacobsohn, "Diabetes Melitus," Dissertation, Rostock, 1896.
10. *Union méd.*, 1872, XIV.
11. *Bull. Acad. de méd.*, 1881.
12. *Gaz. Hebd.*, 1882, 801.
13. Külz, "Klin. Erfahrungen," 1899, 248.
14. "Le Diabète Sucré," Paris, 1909.
15. "Traité du Paludism."
16. *Gaz. Hebd.*, 1882.
17. Quoted by Buhl, *Zeitschr. f. Rationelle Heilkunde*, 1857.
18. *Arch. f. Heilkunde*, 1867, VIII, 331.
19. *Gaz. d. Hôp.*, 1866, 410.
20. *Bull. de la Suisse Rom.*
21. *J. Exper. M.*, 1889, IV, 137.
22. *Boston M. & S. J.*, 1899, 20.
23. *Lancet*, Lond., March 2, 1912.
24. "La Diabète Sucré," 401.
25. *Handbuch d. Kinderh.*, 1883, XIX, 216.
26. *Arch. f. Kinderh.*, 1890, XI, 81.
27. Loc. cit.
28. *Deutsche Med. Ztg.*, 1900, 1211.
29. *Deutsche med. Wchnschr.*, 1906, 25.
30. *München med. Wchnschr.*, 1903, 26.
31. Loc. cit.
32. *Ztschr. f. klin. Med.*, XX, 272.
33. Loc. cit.
34. Loc. cit., page 141.
35. Loc. cit., pages 141, 142, 330.
36. Loc. cit., p. 85.
37. *Wien. klin. Wchnschr.*, 1906, No. 29.
38. Loc. cit.

THE SIGNIFICANCE OF RICKETTSIA IN RELATION TO DISEASE

By Richard P. Strong, M.D.

In 1916 Rocha-Lima called attention to the presence of very minute bodies which were found in lice which had fed upon patients suffering with typhus fever. These bodies were present not only in the contents of the alimentary canal, but especially in the epithelial cells of the alimentary tract of these insects. He regarded them as very minute micro-organisms. They were elliptical, oval, often found in pairs, and bipolar in appearance. The smaller forms measured from about .3 to .4 micron, and the larger ones, sometimes biscuit-shaped, from .4 to .9 micron. They were best demonstrated by staining in Giemsa's solution. These organisms were not at first found in lice which had not fed upon cases of typhus fever. The lice were said to become parasitized only after ingesting infected blood. Rocha-Lima pointed out that while these bodies slightly resembled bacteria in their morphology, they were in other respects more like the *Chlamydozoa strongyloplasmata.* He, therefore, proposed for them the name of *Rickettsia prowazeki* (n.g. n.sp.), evidently choosing this name in memory of Ricketts and Prowazek, both of whom succumbed to typhus fever, which they contracted while pursuing their independent investigations upon this disease. Subsequently, organisms having a similar appearance were found by other observers, and also by Rocha-Lima, in lice which had fed upon healthy individuals or on those suffering with various other diseases. For this second form Rocha-Lima proposed the name of *Rickettsia pediculi.* He believes that *Rickettsia pediculi* differs from *Rickettsia prowazeki* in that the former is found normally only in the lumen of the alimentary canal of the louse, and does not multiply in the cells of the insect's alimentary tract, or does so only exceptionally.

It is of importance in considering the study of the Rickettsia to recall that the terms Chlamydozoa (Prowazek) (1), Strongy-

loplasmata (Lipschutz) (2) were proposed to include a group of very minute pathogenic organisms or viruses which exhibited certain common properties, while exercising specific peculiarities in each case. These viruses are believed during at least one stage of their development (that of the "elementary corpuscles") to pass through bacterial filters without losing their virulence. Within the cells of the host the elementary corpuscles are believed to grow into larger "initial bodies."

The chief characteristics of the Chlamydozoa (3) were said to be first, their minute size, smaller than any bacteria hitherto known, enabling them to pass the ordinary bacterial filters during one stage of their development; second, that they develop within cells, in the cytoplasm or nucleus, and produce characteristic reaction products and enclosures of the cell; third, that they pass through a series of developmental stages, and are specially characterized by their mode of division, which is not a simple process of splitting, as in bacteria, but is effected with formation of a dumb-bell-shaped figure, as in the division of a centriole. Two dots are seen, connected by a fine line like a centrodesmose, which becomes drawn out until it snaps across the middle, and its two halves are then retracted into the body. In appearance the Chlamydozoa seem to consist primarily of merely a grain of chromatin without cytoplasm and without a membrane of any kind. Hence they appear to represent the simplest form of living body. The Chlamydozoa have not yet been successfully cultivated, but infections can be produced with pure colloid-filtrates free from bacteria, but containing the minute bodies themselves. They are characteristically parasites of epiblastic cells and tissues. The viruses of trachoma, vaccinia, scarlet fever, hydrophobia, molluscum-contagiosum, and more recently of typhus fever, have been referred to the Chlamydozoa.

Previous to Rocha-Lima's observations, several investigators besides Ricketts had published articles describing micro-organisms observed in lice which had fed upon typhus fever patients, and Ricketts also described a somewhat similar organism in connection with Rocky Mountain fever. The results of these investigations have been summarized in the following table:

TABLE SHOWING THE PRESENCE OF RICKETTSIA BODIES.

YEAR	INVESTIGATOR	RICKETTSIA BODIES OR ORGANISMS RESEMBLING THEM FOUND IN
1909	RICKETTS	Blood of guinea pigs and monkeys infected with blood from Rocky Mountain spotted fever cases. Also seen in blood of man, and in female tick (*Dermacentor occidentalis*) and in eggs of these ticks fed upon infected guinea pigs.
1910	RICKETTS AND WILDER	Studies in Mexico. Blood of typhus patients. Also in dejecta and various organs of lice fed on typhus patients. Occasionally found in feces and intestinal contents of normal lice.
1910	GAVIN AND GIRARD	Blood of patients in Mexico. Significance of bodies obscure.
1913	PROWAZEK	Blood of 51 typhus cases in Belgrade. In examination of sections of organs of typhus cases, trachoma-like bodies observed in endothelial cells of heart, lung, liver, kidney. One infected louse contained coccoid bodies and diplococcus forms.
1914	SEARGENT, FOLEY AND VIALETTE	Lice living only on the sick, never in lice living on healthy people, or recurrent fever patients, in Algeria. Found especially in bloody fluid of digestive tract of the lice. A number of such lice fed on healthy individuals and proportion of microbes seen became much larger. Could not cultivate micro-organism on artificial media.
1914	NICOLLE, BLANC, AND CONSEIL	Tunis, in 5 per cent of lice collected in districts free from typhus for two years. Lice fed on typhus cases are constantly infectious on ninth and tenth day, not before the eighth. Organisms not detected in blood and organs of guinea pigs infected with typhus.
1915	PROESCHER	Blood smears from nine typhus cases showed bodies in endothelial cells from blood vessels. Very few seen in plasma and in polynuclear leucocytes. These bodies not found in normal blood or in blood from cases of measles, mumps, scarlet fever, cholera, relapsing fever.
1916	DORENDORF	Blood of typhus fever cases in Serbia examined, and organisms described by Prowazek discovered in all cases examined during febrile stage. Found in plasma and in polymorphonuclear and mononuclear leucocytes.
1916	STEMPLE	Among the enigmatic parasites in the intestinal epithelium in dissected lice collected from sick people.

TABLE SHOWING THE PRESENCE OF RICKETTISA BODIES—*Continued.*

YEAR	INVESTIGATOR	RICKETTSIA BODIES OR ORGANISMS RESEMBLING THEM FOUND IN
1916	Lipschutz	Polymorphonuclear leucocytes in blood from typhus cases; 23 examined, 18 were positive. These bodies not found in control preparations from typhoid fever and variola cases, or in normal blood preparations.
1916	Csernel	Typhus blood.
1916	Zollenkopf	In describing a new disease resembling intermittent fever (probably Wolhynian fever) found changes in red cells. Not found in preparations taken after the fever.
1916	Rocha-Lima and Prowazek	Investigations at Prison Camp, Kottbus, 95 per cent of lice taken from sick people were infected by parasitic micro-organism. Organisms found in contents of alimentary canal, and especially in epithelial cells of alimentary tract. Not found in lice living on healthy subjects. Non-infected lice placed on sick patients became infected. This parasite found in man only in leucocytes.
1916	Rocha-Lima	In 1914 (December) in streak preparations made from lice fed on typhus cases, found large numbers of bodies. Recognized by Prowazek as the same as seen by him in 1913 in preparation from infected louse. In examination of sections of lice from typhus cases, and of normal lice, bodies found in large numbers in cells of alimentary canal and in salivary glands of infected lice; not in normal lice; 17 out of 18 lice from a sick patient were infected. Rickettsia appeared in cells of intestine of lice on fourth or fifth day. Louse fed on typhus patient showed Rickettsia four days afterwards.
1917	Munk and Rocha-Lima	Found diplobacillus in blood of Wolhynian fever cases, but also found same in blood from patients with other diseases, or even from healthy ones. Munk made 70 experiments on patients diagnosed as Wolhynian fever cases—51 positive for *R. pediculi*, 11 negative, 6 doubtful. Among negatives were some typical cases. Among 33 control tests, 26 were negative and 6 infected same as lice from Wolhynian fever cases. These 6 cases upon which the lice were fed, which proved positive for Rickettsia, were 3 malaria, 1 bladder disease, 1 bronchitis, 1 inguinal hernia. One normal gave rise to strongly infected lice. Rocha-Lima and Korbsch attempted propagation of Wolhynian fever with lice, but not successfully, although lice were strongly infected.

TABLE SHOWING THE PRESENCE OF RICKETTSIA BODIES—*Continued.*

YEAR	INVESTIGATOR	RICKETTSIA BODIES OR ORGANISMS RESEMBLING THEM FOUND IN
1916	NOLLER	Lice from pigs transferred from infected guinea pigs to pig blood.
1917	TOEPFER AND SCHUESSLER	In 400 lice which had fed on 35 patients, bacteria-like organisms were found in the infected lice. Organisms found constantly in intestinal canal and of lice removed from typhus patients, and often in cells of alimentary tract. Control lice fed on other individuals than those suffering with typhus fever remained free. Organisms found only in lice fed on blood of typhus patients during febrile (not post-febrile) period.
1916	TOEPFER	Blood of Wolhynian fever. Also in lice from typhus fever patients. Lice from typical Wolhynian fever contained bodies in alimentary tract similar to typhus fever organism. Bodies both free and inside the cells.
1916	TOEPFER	Examined smears and sections of 500 lice. Confirmed his former observations regarding organism in infected lice. Same parasite found in lice from head of patients and artificially infected normal lice of this species by placing them upon the sick. Smears from lice fed on typhus blood contained organism. Described intracellular diplobacilli in tissues of typhus patients.
1916	HANSER	Confirms Toepfer's discovery of forms in intestinal cells of lice fed on typhus patients.
1917	TOEPFER	In article on war nephritis describes similar organisms to those seen in lice fed on cases of typhus or Wolhynian fever. Found similar organisms in three diseases, i.e., spotted fever, Wolhynian fever, and nephritis.
1917	OTTO AND DIETRICH	In lice placed on patients. Infection not hereditary. They infected lice with Rickettsia by feeding them on a case of typhus fever without the exanthem.
1916	WOLBACH	Bacillary bodies are present in large numbers in endothelial cells of guinea pigs infected with the virus of Rocky Mountain spotted fever through the bites of infected ticks.
1916	WOLBACH	Organism found in experimentally infected ticks, similar to those previously seen in tissues of monkeys and guinea pigs, but never in non-infected ticks. Parasites most abundant in striped muscle, Malpighian tubes, salivary glands, and ducts and brain ganglia. Numerous in muscle fibers of uterus and vagina, and seen in the spermatozoa. Also in lesions of blood vessels in fatal human cases of Rocky Mountain spotted fever.

TABLE SHOWING THE PRESENCE OF RICKETTISA BODIES—*Continued.*

YEAR	INVESTIGATOR	RICKETTSIA BODIES OR ORGANISMS RESEMBLING THEM FOUND IN
1912	DOEHLE	Discovered intra-leucocytal bodies in scarlatina cases.
	PREISICH	Recognized same bodies in other diseases.
1917	LOPEZ	Blood of typhus fever, found same intra-leucocytal bodies, in 77 cases out of 90. Blood must be taken from well-marked cases and at the height of the fever, to contain these bodies.
1917	SCHMIDT	Organisms found in 3 cases only, out of many cases of five-day fever examined.
1917	JUNGMANN AND KUCZYNSKI	Blood of typhus patients during first days of the rash, and also in trench fever. Had never found organism in other diseases.
1917	WERNER AND BENZLER	In the stomach of lice fed upon cases of febrisquintana.
1918	BRUMPT	53 out of 72 body lice taken from healthy prisoners of war, pure culture found in the alimentary canal and in some cells; 16 lice from healthy prisoners of war were all infected, etc.
1918	ARKWRIGHT, BACOT, AND DUNCAN	Lice fed on trench-fever patients. Normal lice fed on persons not exposed to trench-fever infection remained free from Rickettsia.
1914	RABINOWITSCH	In 1908 discovered *Diplobacillus exanthematicus* as the causative agent of typhus. Organism found in blood of typhus patients.
1913	MULLER	Blood of typhus fever cases, inoculated mice and rabbit.
1918	KUCZYNSKI	In the petechiæ of typhus cases, in sections of liver in the endothelial cells of the capillaries, and in free phagocytic cells.

Our studies regarding the occurrence of Rickettsia bodies in lice which have fed upon healthy persons have confirmed those of a number of observers already referred to. Lice collected from healthy men in different parts of France where neither typhus fever nor trench fever were present were often found to contain Rickettsia in their dejecta, from 20 to 40 per cent of such lice examined, collected in different groups, revealing these bodies. In some of these normal lice, microscopical examination of the excreta or material from the alimentary tract showed them to be severely infected with Rickettsia bodies. Others were only moderately or very slightly infected, while in the remainder no definite Rickettsia were observed. Obviously, from a microscopical examination, it is some-

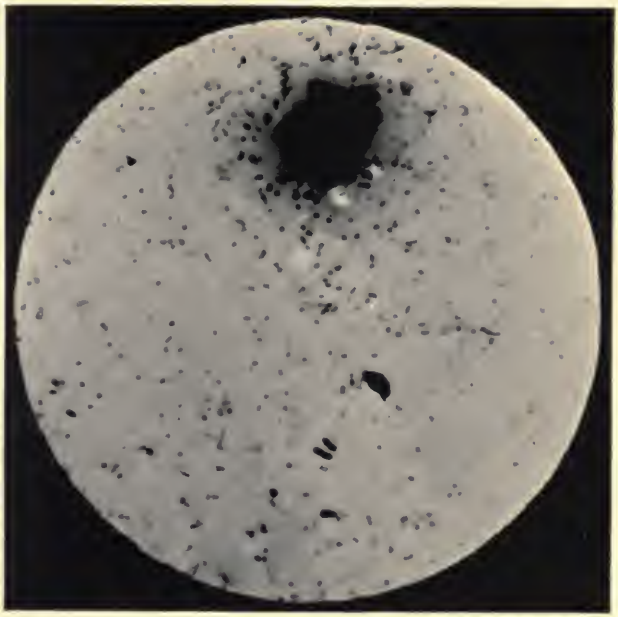

Fig. 1.

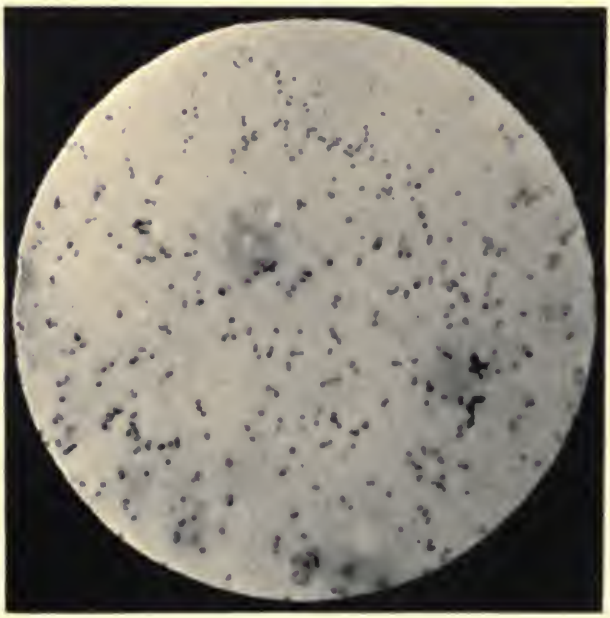

Fig. 2.

Plate I.—Richettsia Bodies in the Excrement of Normal Lice.

times extremely difficult to say whether these bodies are not present in small numbers in the lice. In Plate I, Figs. 1 and 2 demonstrate the Rickettsia bodies in the excrement of *normal* lice.[1] The lice are referred to as normal because they produced no disease either in their original host, from which they were collected, or when they were placed upon or fed upon other healthy individuals.

A critical examination of the literature regarding the relation of Rickettsia to disease reveals the fact that these bodies have been found in lice which have fed upon cases of typhus fever, Wolhynian fever, trench fever, war nephritis, malaria, bronchitis, inflammation of the bladder, and inguinal hernia, as well as in a large number of lice collected in different parts of the world which have fed only on healthy people, in whom they produced no disease. It is true that in lice, Rocha-Lima suggests that *Rickettsia prowazeki*, which is regarded by him as the probable cause of typhus fever, differs from *Rickettsia pediculi*, which is found in lice not infected with the virus of typhus, in that the latter does not occur normally in the epithelium of the alimentary canal of the louse. However, Toepfer, Brumpt, and others, as we have seen, have found Rickettsia in the intestinal epithelial cells of lice fed upon healthy individuals, as well as in those fed upon Wolhynian fever cases and cases of war nephritis. Rickettsia have also been found in ticks that have fed upon cases of Rocky Mountain spotted fever. They have, in addition, been observed in the blood of man in a number of diseases—for example, in typhus fever, in Rocky Mountain spotted fever, in Wolhynian fever, and in trench fever. Rocha-Lima also believes that he has seen in the blood of healthy persons bodies similar to those observed in the blood of Wolhynian fever by other investigators, and described by them under the name of Rickettsia.

Further, when we come to consider the etiological significance of Rickettsia in human disease, it is apparent, from the evidence already presented in this article, that not one of the three classical postulates regarded necessary for the proof of the etiological factor of an infectious disease is fulfilled by the Rickettsia. (1) They have not been found in every case of the disease they have been said to

[1] These photomicrographs were kindly made at the Pasteur Institute by Dr. P. Jeantet, who is in charge of the photomicrographic work of this Institute. I wish to express my thanks both to Dr. Roux, the Director of the Pasteur Institute, and to Dr. Jeantet for this courtesy.

cause; moreover, they have been found in connection with other diseases than the one of which it is contended they are the source. (2) They have not been isolated and grown in pure culture. (3) The disease which they are said to cause has not been produced by the inoculation of such culture.

It is very possible that the Rickettsia bodies are micro-organisms, but as they have been found in lice from patients with so many different diseases, as well as in lice from healthy individuals, obviously no specificity for them can be justly claimed at the present time. It is true that Rocha-Lima, Toepfer, and Olitsky, Denzer, and Husk claim to have produced typhus infection in animals by the inoculation of the contents of the alimentary tract of infected lice. In this connection Rocha-Lima claimed that the disease developed in the inoculated animal because the Rickettsia were present in the lice used for the injections, while, on the other hand, Olitsky, Denzer, and Husk claim the disease developed because the Plotz bacillus was present in the lice used in the inoculation of the animals. Obviously we can draw no definite conclusions from these experiments save that the infecting agent, visible or invisible, was present in the lice. Nothing can be said from them regarding the definite nature of the infecting agent. Seargent, Foley, Vialette, and Brumpt all pointed out that the Rickettsia might merely accompany the infectious agent.

Some further light has recently been thrown upon the significance of the Rickettsia by observations and experiments which we have made in connection with trench fever. In relation to the etiology of trench fever, as has been the case in the history of most infectious diseases, a number of widely differing micro-organisms have previously been described as its cause, but none of these claims has been substantiated, and, although very extensive studies have been made by a large number of observers, it is still a question whether the organism causing trench fever has yet been definitely seen in man, either with the microscope or the ultramicroscope. Our experiments, carried on in relation to the etiology of trench fever, have since shown that this disease is caused by a filterable virus, which bears some resemblance in its behavior to the filterable virus of hog cholera (4). Our work regarding the filterable qualities of the virus of trench fever has recently been confirmed by Major-General

Sir John Rose Bradford, Captain E. F. Bashford, and Captain J. A. Wilson (5). The organism causing trench fever, being so minute, is obviously separated only with great difficulty from the surrounding structures in the media in which it occurs naturally. Thus, while we have demonstrated that the virus of trench fever is present free in the plasma of the blood of trench-fever cases, in the febrile stages of the disease it is frequently very difficult to separate it from the blood corpuscles themselves by repeated washings of these with saline solution (6). Also, in the alimentary canal of the louse fed upon trench-fever cases and in infected louse excrement, the virus, on account of its minute size, is closely intermingled with other cellular structures present.

We have also emphasized the fact that in different examinations of lice fed only upon healthy individuals, the Rickettsia have been demonstrated in from 20 to 74 per cent. Knowing these facts, let us suppose that lice already containing such Rickettsia in variable number had been fed upon trench-fever cases and had become infected with the virus of trench fever, and such lice (containing the Rickettsia, which may in the meantime have multiplied or increased in number) were then placed upon healthy human beings, whom they subsequently infected with trench fever, obviously, then, erroneous conclusions might be drawn that the Rickettsia were themselves the etiological factor of trench fever. It is evident that great difficulty would be experienced in a separation of the virus of trench fever from such bodies under the circumstances described above. Probably only by successful filtration experiments such as we have performed with lice excrement in connection with trench fever could the separation be accomplished.

It may, of course, be argued that Rickettsia have a filterable stage, as have other so-called Chlamydozoa, and this idea receives some support from the fact that the virus of trench fever is under some circumstances filterable with difficulty, and attempts to infect human beings with the filtrates of infected material are often unsuccessful. Thus in 10 filtration experiments performed with infected blood and urine from trench-fever cases, and infected louse excrement, only 3 gave undoubted positive results. The temperature charts of 2 cases of trench fever, experimentally produced by the injection of the filtered trench-fever virus, are illustrated in Plates II and III.

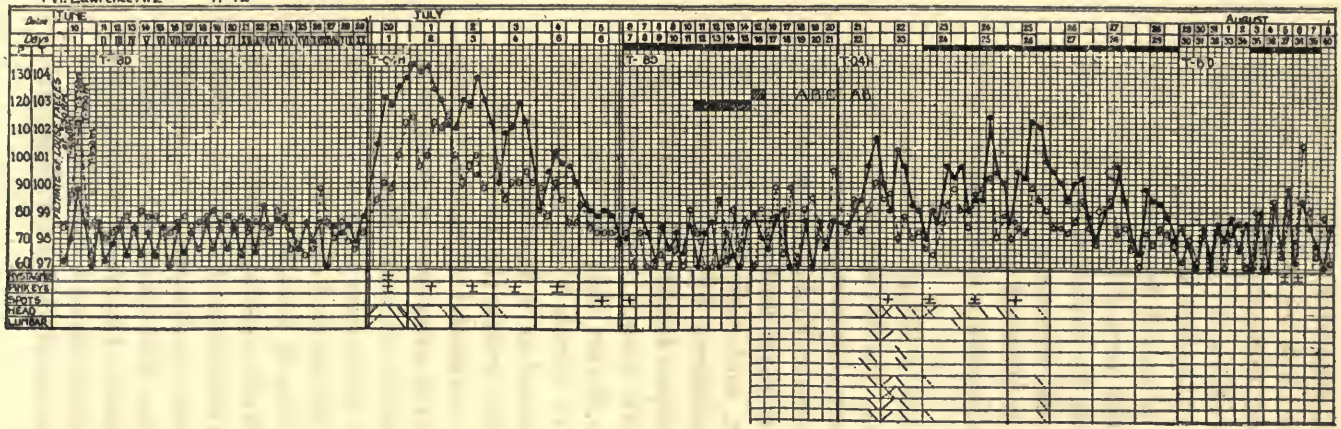

PLATE II.

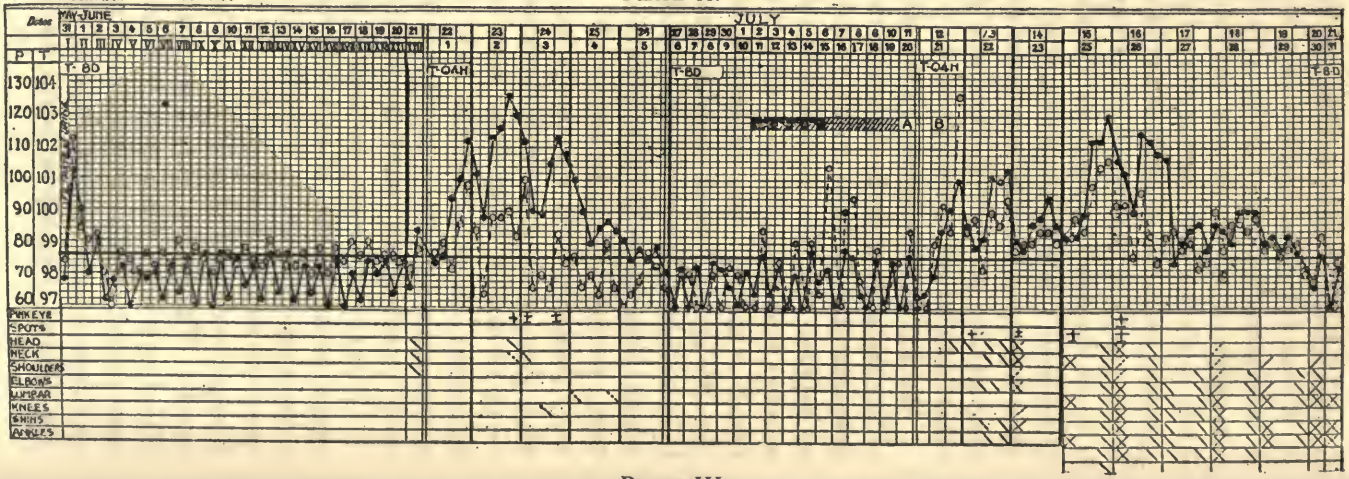

PLATE III.

Bradford, Bashford, and Wilson (7) have since reported upon the cultivation of the trench-fever virus from filtrates which have previously passed through porcelain filters, and have also shown by human experiments that such filtrates contain the infections agent.

It is conceivable that the Rickettsia, whether they possess a filterable stage or not, may be parasites of lice and not pathogenic for man, and Brumpt has suggested that the finding of them in human blood may simply be an indication that the individual has been previously infested with lice. On the other hand, there is the possibility that the bodies sometimes described as Rickettsia may constitute products of degenerated cells—for example, basophilic gradules, which are more numerous in the blood in certain febrile diseases, in which case they would also increase in number in the lice fed upon such cases, and might then merely accompany the very minute or invisible etiological factor of the disease.

In connection with the significance of Rickettsia as an etiological factor in typhus, trench fever, and other diseases, it may be of interest to recall that in 1903 an organism described by Parker, Beyer, and Pothier as *Myxococcidium stegomyiæ* was found in infected stegomyia mosquitoes, and was for a time supposed by these investigators to be the parasite causing yellow fever. Later this organism was found to be a species of yeast, and to occur not only in mosquitoes infected with the virus of yellow fever, but also in those not infected with such virus, and the virus of yellow fever was shown to be filterable and ultramicroscopic. Noguchi's (8) recent experiments, however, suggest that the organism of yellow fever may be a spirochæte which is filterable at least at one stage of its life history.

From a review of the evidence presented in this paper regarding Rickettsia, it appears obvious that, until more definite results are obtained from further experimental work, we are not justified in concluding that the Rickettsia have a definite specific etiological significance in relation to human disease.

BIBLIOGRAPHY

1. *Arch. f. Protistenk.*, 1907, X, 336.
2. "Handbuch de Pathogenen Protozoen," Leipzig, 1911, Prowazek and others.
3. Minchen, "Introduction to the Study of the Protozoa," London, 1917, 472.
4. "Trench Fever; Report of Commission of American Red Cross Research Committee," Oxford, 1918.
5. Bradford, Bashford, and Wilson: *Brit. M. J.*, 1919, 127.
6. Loc. cit., "Trench Fever Report," 27.
7. Bradford, Bashford, and Wilson, loc. cit.
8. Noguchi, *J. Am. M. Ass.*, 1919, LXXII, 187.

THE RELATIVE INFREQUENCY OF CANCER OF THE UTERUS IN WOMEN OF THE HEBREW RACE

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In a short paper on the "Etiology of Cancer of the Pelvic Organs," read before the New York Obstetrical Society (1), January 9, 1906, the writer drew attention to an observation he had made during a service of fifteen years in Mount Sinai Hospital Dispensary. Although the service was a large one, visited by the class of women that ordinarily should furnish a fairly large number of cases of cancer of the uterus, he was struck with the rarity with which that disease was encountered. Being cognizant of the almost universal opinion that laceration of the cervix was a potent cause of cancer of that organ, he paid especial attention to all cases with reference to that point. Every case presenting the slightest suspicion of malignancy was subjected to a thorough examination and kept under observation for a long period afterwards to determine the correctness of the microscopic report. It may, therefore, be fair to assume that very few cases escaped detection. This assumption receives further confirmation from the fact, to which the writer has frequently drawn attention, that it is very rare indeed that one meets with cancer of the cervix, especially of the vaginal portion, the most common variety, in which the diagnosis is not unmistakable on palpation and inspection with the naked eye. In other words, when cancer of the cervix gives rise to symptoms, it is almost always so far advanced that the diagnosis is positive without the aid of the microscope. The suspicious cases, as a rule, with very few exceptions, prove not to be such. That, at least, has been the writer's experience and that of a good many other gynecologists with whom he has spoken.

The data, therefore, regarding this point, which the writer collected from his Dispensary service from 1893 to 1906, a period of thirteen years, may be regarded as approximately accurate. There were during this period 19,800 new patients. Among these

there were 1995, or about 10 per cent, with marked laceration of the cervix. There were in all 18 cases of cancer of the cervix. Here comes the strikingly interesting point: Roughly speaking, 95 per cent of the patients were of the Hebrew religion and natives of Russia, Austria, and Poland. Still of the 18 cases of cancer of the cervix only 9 cases, 50 per cent, occurred among this class of patients, while the other 9 cases were met with among the non-Jewish women, who constituted only 5 per cent of the patients. Consequently the incidence of cancer of the cervix was twenty times greater in the non-Jewish than in the Jewish women. When one stops to consider that of the total number of the Jewish women 1995 had badly lacerated cervices, that they were all immigrants who, according to Max Schüller, (2) show a much greater predisposition to cancer than do the natives, and that they were living in the worst possible hygienic surroundings, amidst the greatest squalor and privation, such as obtain in the lower East Side of the Metropolis, it is truly remarkable that so few cases of cancer of the cervix were detected amongst them.

My associate and friend, Dr. I. C. Rubin, made a painstaking investigation of the cases in all of the gynecological services in Mt. Sinai Dispensary from December, 1909, to December, 1918—a period of nine years.

The total number of new cases examined approximated 30,000. Total number of positive cases of cancer of the cervix was 20. Total number of suspected but not established cases of cancer of the cervix was 50. This included hypertrophied, eroded, ulcerated, and bleeding cervices in which subsequent control failed to establish cancer, or in which curettage, partial excision of the cervix for diagnostic purposes and hysterectomy did not result in a positive finding of cancer. The proportion of cases of cancer of the cervix in this material was therefore 20 in 30,000, or 1 in 1500 cases. Of these 20 cases 13 were in Jewish women and 7 in non-Jewish women. The 7 non-Jewish women were either Americans or of the Slavic immigrant class.

The general proportion of non-Jewish to Jewish women at the Dispensary during this period was about one in 15,[1] consequently the actual incidence of cancer of the cervix in the Jewish patients of the Dispensary was 13 in 28,000, or 1 in 2154 cases. In the non-Jewish women it was 7 to 2000, or 1 in 285, or 7½ times greater than in the Jewish women.

[1] Based on an actual count for two years of the period.

It is interesting to note the close ratio of the incidence of cancer of the cervix in the Jewish women in the two series, that of 1893–1906 and of 1909–18. In the one it was one in 2089 cases, in the other one in 2154 cases. But the ratio in the non-Jewish women shows a marked difference. In the first series it was one in 111 cases, in the second series it was one in 285 cases.

Dr. Rubin investigated also the records of the Mt. Sinai Hospital during the same period. From December, 1911, to December, 1918, there were: Carcinoma of the cervix, 58 cases; of the uterus, 35 cases; of the vagina, 5 cases. The total number of patients admitted to the Gynecological Department during this period was approximately 7000. The total number of adult females admitted to the hospital during the same period was 30,000. As each of these patients was subjected to a thorough and careful physical examination as a matter of routine, and wherever the slightest suspicion existed a special gynecological examination was added by one of the attending gynecologists, it is quite natural that the percentage of cancer of the cervix would be much higher than in the dispensary cases. The difference in the ratio can further be explained by the fact that practically only operative cases are admitted to the gynecological services of the hospital.

But the point that has a special bearing upon our contention is the ratio existing between the non-Jewish and Jewish women. Of the 65 cases of cancer of the cervix 32 were in Jewish and 33 in non-Jewish women. As the same ratio obtains in the hospital[2] as in the dispensary, that is, 1 to 15, the general incidence would be for

Jewish women, 32 to 28,000, or 1 in 937 cases.
Non-Jewish women, 33 to 2,000, or 1 in 61 cases.

The incidence therefore is fifteen times greater in the non-Jewish patients than in the Jewish patients treated in the hospital.

Occurrence of Carcinoma in Other Viscera. For this purpose the year December, 1917, to December, 1918, was chosen.

Carcinoma of the rectum, 23 cases: Jewish, 21; non-Jewish, 2. In this series there were 9 in females and 14 in males.

Carcinoma of the intestines, 23 cases: 11 in females, 12 in males, 19 Jewish, 4 non-Jewish, of which 3 were females.

Carcinoma of the stomach, 43 cases: 18 females, 25 males, 37 Jewish, 6 non-Jewish, 4 women and 2 men.

Carcinoma of the breast, 17 cases: 6 non-Jewish.

Contrasted with the occurrence of carcinoma in other organs than the uterus, it appears that carcinoma of the cervix is a little more than eight

[2] Based on an actual count for two years of the period the same as for the dispensary.

times as infrequent as carcinoma of the rectum; eight times as infrequent as carcinoma of the intestines, exclusive of the rectum; sixteen times as infrequent as carcinoma of the stomach, and about seventeen times as infrequent as carcinoma of the breast.

In other words, there are treated as many cases of carcinoma of the rectum or of the intestines *in one year* at Mt. Sinai Hospital as there are carcinoma of the cervix uteri cases in eight years, and twice as many stomach cancer cases in one year as there are cancer cervix cases in eight years.

This is highly significant in view of the fact based on statistics (references to which occur later) that in the relative frequency of cancer of the individual organs, that of the uterus stands first in the list.

The writer has made a search of the literature and found but very meager references to the subject. What he did find was all confirmatory. After the time the writer made the observations here under discussion he interrogated several colleagues who were likely to come into contact with the same class of patients. They all said that since their attention had been drawn to it, they recalled that their experience corresponded with his own.

A. Theilhaber (3) draws attention to the slight disposition of Jewesses to cancer of the cervix. In 228 cases of fibromyoma 49 (19.1 per cent) were Jewesses; in 133 cases of cancer of the cervix only 1 (0.75 per cent) was a Jewess. He learned that this experience was confirmed by others.

F. Theilhaber (4) states that disease statistics in Germany are not classified according to religion. But such a classification exists in the city of Budapest. In that city the Jews are fairly equally divided among all classes of inhabitants. They show a marked increase of births over the others. He furnishes statistics to demonstrate that the number of childbirths have a bearing upon cancer of the cervix.

No. of Births	Cancer of the Cervix, Per Cent	Fibromyoma, Per Cent
0	4	39
1	13	19
2	15	13
3– 5	33	19
6– 8	15	9
9–10	10	1
11–15	10	0

Hofmeier and others have published statistics demonstrating a similar ratio between the number of childbirths and the occurrence of cancer of the cervix.

Theilhaber emphasizes the significance of the fact that Jewesses reach an older age than do other Budapest women. Hence their participation in all diseases in which age bears an influence should be greater. He states that the mortality among Jewish children is much less than among other children. This, of course, as a natural consequence advances the age of the Jewish population, so that under the Jewish deaths almost double as many old people are to be found as under the deaths of all the other population.

To quote further from Theilhaber's paper, in the year 1906 there were in all 16,360 deaths in Budapest, among which were 2500 Jews, or 15 per cent; 27 per cent, excluding cancer of the uterus, died of cancer, but only 8.05 per cent died of cancer of the uterus; thus there were only one-third of the number which one would expect from the cancer deaths *in toto*.

DEATHS IN BUDAPEST

Year	Total Deaths	Jewish Deaths	Total Cancer Deaths	Jewish Cancer Deaths
1906	16,380	2,500	785	183
1905	16,094	2,623	867	153
1904	15,435	2,614	1,009	192
1903	15,059	2,468	896	188
1902	14,732	2,400	869	167

DEATHS FROM CANCER OF UTERUS

Year	Total	Jewesses, Per Cent	Jewish Cancer Deaths Per Cent
1906	149	12— 8	23·3
1905	142	15—10·5	17
1904	170	13— 7·7	19
1903	150	18—12	20·9
1902	172	10— 5·8	19·1
	783	68— 8·7	19·5

There is no separation in the above statistics of cancer of the cervix from that of the body, so that many of the cases may have been cancer of the body.

Theilhaber quotes from H. Kirschner unpublished data in reference to the city of Munich. In that city from 1876 to 1908 there died 185 Jews from cancer, of these there were 98 women. Seven of

these had cancer of the uterus, so forming only 7 per cent of the cancer cases in the Jewish women. The usual ratio of cancer of the uterus is from 25 per cent to 35 per cent of all cases of cancer. That the Jewesses of Munich did not show such relative immunity from cancer of other organs is evidenced by the fact that during the same period 41 died of cancer of the stomach and of the intestines.

Birch-Hirschfeld has asserted that the relative frequency of cancer of the individual organs may be stated according to the following scale: 1, Uterus; 2, external skin; 3, mamma; 4, stomach.

A. Theilhaber and S. Greischer (5) furnish further statistics from Munich and Nürnberg:

MUNICH, 1907–1909

Christians

		Per cent
Total No. of deaths	1326	....
No. of deaths from cancer of uterus and mamma	501	37.7
No. of deaths from cancer of uterus	381	28.7
No. of deaths from cancer of mamma	120	9

Jewesses

Total No. of cancer deaths	102	23.5
No. of deaths from cancer of uterus	7	6.8
No. of deaths from cancer of mamma	17	16.7

NÜRNBERG, 1907–1909

Jewesses

Total No. of cancer deaths	30	....
No. of deaths from cancer of uterus and mamma	6	20
No. of deaths from cancer of uterus	1	3.3
No of deaths from cancer of mamma	5	16.6

It will thus be seen that in Munich the percentage of deaths from cancer of the uterus among Jewesses was but one-fifth of those among the Christians. On the other hand, the percentage of deaths from cancer of the mamma among Jewesses was nearly double as great as that among Christian women.

The writer consequently believes that the fact has been fully established that cancer of the cervix of uterus is much less frequently met with among Jewesses, particularly of those belonging to the poorer classes and hence among the most orthodox, than among the women of the Christian religion.

The fact has also been established that so far as cancer of the other organs is concerned no such immunity exists. On the contrary, if anything, statistics demonstrate that Jewesses are more prone to cancer of the other organs than are their Christian sisters.

The question now arises, to what factor or factors may be attributed the comparative immunity of this particular organ? What is there in their mode of living and habits that stands out prominently as being different from the poorer classes of other religions? No explanation, as far as the writer is aware, has been offered by any of the authors who have written on the subject. We know that whatever differences there may exist regarding squalor, poverty, and unhygienic surroundings are not in their favor.

The writer himself in the article referred to ventured an explanation. It occurred to him that the only marked difference in their mode of living and habits from that of the women of most all other religions consisted in their strict observance of the Mosaic Law regarding marital relations. Sexual congress is prohibited during menstruation and during seven days following the cessation of the flow. The Mosaic Law[3] commands that the woman count seven unclean days (whether the flow lasts that long or not) and seven clean days before she takes the bath of immersion and marital relations are resumed. If the flow should persist for more than seven days or return before the count of the seven clean days had elapsed, the count of the seven clean days must begin anew. Thus in cases of menorrhagia or metrorrhagia sexual intercourse might not be permitted for months.

Again after parturition the Mosaic Law[4] enjoins abstinence from the sexual act for a variable period, depending upon whether the birth was of a male or female child. My learned friend Dr. D. de Sola Pool states that these laws are only the starting points for an extended development in actual Jewish life—"one-sixth of the whole Talmud is given up to laws of women, including the laws of marriage,

[3] Leviticus xv, 19 seq. [4] Leviticus xii.

divorce, etc., and the laws in which you are especially interested." He further states the official formulation of Jewish law compiled towards the end of the Middle Ages, which is still the authoritative code of traditional law, "demands the counting of fourteen days for a male and twenty-one days for a female child before the woman is permitted to her husband." "There are places where it is the custom not to take the bath of purification after childbirth until forty days after the birth of a son and eighty days after the birth of a daughter. It has become the general rule throughout Israel not to cohabit so long as there is any blood whatsoever, even 'clean blood.' Therefore, if there is any appearance of blood after seven or fourteen days, even though the Biblical law allows cohabitation, it is customary to wait for seven complete days after the disappearance of the last vestige of blood before allowing cohabitation."

It is well known that the poorer classes of non-Jewish women not only do not observe such restrictions, but are in the habit of indulging in cohabitation during the menstrual period and very shortly after parturition.

If there is one thing in which there is a consensus of opinion regarding the etiology of cancer it is that continued irritation, especially under unfavorable conditions, is a potent causative factor. That sexual irritation under any condition is a predisposing cause is evidenced by the fact, established by all available statistics, that cancer of the cervix is much more common among the married and widowed than among the non-married.

Accepting this proposition, then, it must be granted that cohabitation during the menstrual period or immediately thereafter, when the uterus is still in a high degree of congestion, must increase markedly the harmful effect of the irritation of the sexual act at ordinary times. It must be borne in mind, in consequence of their adherence to the Mosaic Code, the orthodox Jewish woman is subjected to this irritation of the sexual act for practically only two weeks out of four. And that in cases of metrorrhagia (having to count seven clean days) the sexual act may not be allowed for months at a time. That sexual intercourse after parturition before the bloody discharge has ceased must cause hyperirritation must also be granted.

The writer is fully aware that the theory he offers does not permit of substantiation by scientific experimentation. But in our present ignorance of the cause of cancer a collection of carefully sifted clinical data regarding an organ ordinarily prone to cancer may prove of some value in the solution of the problem of cancer etiology.

BIBLIOGRAPHY

1. *Am. J. Obst.*, 1906, LIII, 410.
2. *Arch. f. Rassen- u. Gesellsch. Biol.*, Bd. I, 1904.
3. *München. med. Wchnschr.*, 56, No. 25.
4. "Zur Lehre von dem Zusammenhang das Sozialen Stellung und der Rasso mit der Entstehung der Uterus Carcinoma," *Ztschr. f. Krebsforsch.*, 1909–1910, VIII, 460.
5. *Ztschr. f. Krebsforsch.*, 1910, X, 530.

THE CONTRIBUTION OF MODERN PSYCHIATRY TO GENERAL MEDICINE

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THE history of psychiatry, like the history of all scientific progress, has been a history, at first, of attempts to describe, to set forth, to define the material with which it was concerned. This descriptive stage in its development has been, perhaps, unusually prolonged because of the great complexity of the problems involved and the inadequacy of the existing knowledge of the nature and meaning of the human mind and its placement in the biological scheme of evolution. Mind, the most intimate and personal of our possessions, has, longer than any other, resisted the application of rigid scientific methods, and its pulling apart, its dissection, has been resented for a longer time and with prejudices equally as strong as those which offered such obstructions to the study of human anatomy.

Until the present generation the scientific approach to the problems of mental disease was by way of an ever-increasing refinement of the descriptions of disease types. The early descriptions had very few concepts to work with in this task, and they were but crude generalities, such as melancholia, mania, and dementia. Upon this simple background classifications were built which largely tended to further divisions based upon the content of the delusional and hallucinatory systems. With such notable exceptions as paresis (first described by Willis, 1672), the attempt to formulate paranoia by Heinroth, and later by Esquirol in his concept of monomania, later followed largely by the English school in this particular, and hebephrenia by Kahlbaum (1863), and later by his pupil Hecker (1871), and the later description of catatonia by Kahlbaum (1869), psychiatry entered upon its career at the beginning of the present generation with only such a simple descriptive material.

During the latter part of the nineteenth century several efforts were made to expand beyond the limitations of such concepts,

notably by Ziehen, who attempted a classification of mental diseases based upon a normal psychology. But as psychology was itself still in the descriptive stage of its development, the attempt only succeeded in further refinements of the various classificatory divisions, which were soon found to have little to commend them because they only rested upon superficially observable differences. Wernicke attempted a neurological approach based upon analogies to aphasia, which also was soon lost sight of, largely, at least, because of the very inadequate knowledge, then, as now, of the real fundamental meanings to be attached to this extremely complex and inadequate concept. Finally Kraepelin, by pushing the life history method of biology to include the course and outcome of the disease, its longitudinal section as opposed to the hitherto cross-section method of study, brought psychiatry to the last refinement of the descriptive stage of its development.

While Kraepelin was elaborating the description of the psychoses, the French school, headed by Janet, was devoting its attention to a finer analysis of the neuroses and psychoneuroses, a movement which was soon followed in this country by a recognition that the place to begin, in order to get an understanding of mental illness, was in the borderland region between health and disease, a principle that was definitely incorporated in the program of the Pathological Institute of the New York State Hospitals. The work done by the students of these borderland states resulted in the formulation of the concept of dissociation, although the dynamics of dissociation were not adequately appreciated and the concept, for the most part, was employed as a still further refinement of description.

About this time there arose the behavioristic school of psychologists, which was the result of attempting to study animal behavior. Inasmuch as animals cannot be interrogated as a means of access to introspective material, the effort here was to apply the methods of objective science to the explanation of conduct. The behaviorists accordingly thought that the best way to answer the query as to what an individual was doing was, not to ask him, for his answer might well be for many reasons misleading, but to observe, as a matter of fact, what he actually did do. Some of the behaviorists actually abjure the introspective data entirely. Out of this behavioristic method of approach have grown those methods of mass

testing, so much used with the military recruits, and those methods of testing out the fitness of individuals for special kinds of work which have received their application in the industrial utilization of prisoners and similar applications in the field of vocational psychology.

About the same time that the behavioristic program was being formulated the psychoanalytic school came into prominence with its exquisite emphasis upon the individual material. It caught up in its principles both the behavioristic concepts, and those of the French school of Janet and its American offshoot. It laid particular emphasis upon the material derived from introspection, not because of its face value, but because it included certain facts of experience, which, because they were psychological facts, were none the less facts and worthy of scientific attention and attempts at explanation. It, too, sought to go beyond purely descriptive aims and attempted an interpretation along lines of dynamic explanations which took into consideration the psychological motives for conduct, not alone those that were obvious, but the deeper-lying motives that could be traced only through an intimate knowledge of the lines along which the personality had developed and unfolded itself. In its technical procedure it emphasized the developmental aspects of the psyche by attempting, as the term psychoanalysis implies, a psychological analysis, dissection, which would disclose the roots through which the symptoms gained the nutrient material which at once called them into being and served to maintain them.

The important contributions of this approach to the problems of defective personal adjustments were the elaboration of the concept of the subconscious as used by the exponents of dissociation and the formulation of the concept of the unconscious which was conceived of as containing the deposits, so to speak, which testified to the history of the development of the psyche, both ontogenetic and phylogenetic. A study of these deposits of the past has by analogy been termed paleopsychology (Jelliffe). Added to this extremely and pragmatically useful dynamic concept of the unconscious is the further concept of the intrapsychic conflict which explains development as a progressive overcoming of obstacles, the nature of which determines the psychological deposits, precipitates, that paleopsychology uncovers for the purpose of discovering the

dynamic elements which have been operative in the formulation of the personality.

The personality is thus seen to be an end product in a continuous series of developmental changes, and conduct to be the final result in action as determined by the historical past of the psyche. The psyche thus comes by analogy to have both an embryology and a comparative anatomy, but instead of bodily organs ideas and feelings, a study of the development of which is of equal importance to its understanding, as are the study of embryology and comparative anatomy to an understanding of the bodily organs.

The study of individual reactions from this point of view soon disclosed that they have protective, defensive, compromise, and substitutive functions, just as we find reactions to have in the realm of the so-called organic, and thus from the point of view of their meanings, the ends that they seek to bring to pass, the distinction as between so-called organic, somatic reactions and so-called functional, psychological reactions tended to be dissolved, broken down, as no longer serving a useful purpose.

This breaking down of the ages-old distinction between mind and body was but the negative aspect of what soon became a movement in a positive direction to construct a formulation that would serve to explain the placement and meaning of the psyche in the developmental scheme. It was the beginning of a union which is already pregnant with great possibilities.

The parallelistic theory of the relation of body and mind, which had occupied the stage for so long, conceived of mind as something which had somehow been added in the course of evolution, and seems to hark back to those medieval concepts that set man apart from the rest of animate creation. The psyche, like disease, was a sort of visitation that came and settled upon man from without, and did not seem to constitute an organic, structural part of his being. A study of the development of the lower forms of life along the lines suggested by Child has served to demonstrate that development has not proceeded by a series of superpositions. He has shown in his study of the development of certain fresh-water planarians the existence of what he variously calls a dynamic, irritability, or metabolic gradient that is a definite organization along certain lines along which the rate of metabolic changes showed a clear

tendency to vary in a gradually decreasing ratio. Living beings, by virtue of the very fact that they are living and are organized, show the existence of their organization in this laying down of gradients, and the main axial gradient shows from the very first a differentiation into a head end. He further demonstrated that these developmental gradients are but the organized interrelations of the several parts of the organism laid down in the structure of the gradient. In other words, the various adjustments which the organism is called upon to make in its relation to its environment, its functions, are integrated and laid down in the structure of its several dynamic gradients: "We must seek for the integrating factor in the relation between living protoplasm and its environment." To illustrate: let a difference at some point in the environment act as a stimulus at a given point at the surface of a bit of protoplasm. The immediate result is an increase of activity at this point which activity is not limited to the point of application, but spreads in ever widening waves such as result when a stone is thrown into a quiet pond. As this wave of energy spreads there is a constant decrement in its effectiveness so that a dynamic gradient is established, the point of greatest intensity or highest rate of activity being the point of the original stimulus. A passing stimulus produces only a passing gradient, while a long-continued, or often-repeated, or very strong stimulus, or all combined, tends to establish permanent changes in the protoplasm along the path of the increased activity. This dynamic gradient becomes the starting point of a permanent quantitative order in the protoplasm or a physiological axis. This is the process which I have called the structuralization of function; it is the organization of past experience made into a stable foundation for further building. The correlation of the several parts of the organism, its integration, is dynamic, and dominance is dependent upon transmitted change or excitation from the region of highest metabolic rate—the head region. The nervous system is "the final expression of relation which is the foundation and starting point of organic individuation."

From this dynamic point of view of the constitution and development of the individual it can be readily appreciated that it is no longer permissible to think of the psyche as something which has been added in the course of evolution. The history of the psyche,

far from being relatively a short one as compared to the history of the body as ordinarily conceived, must of necessity be of equal length. Just as the potentialities of the later developed heart, lungs, liver, kidneys, stomach, etc., were included in the earliest reaction, mechanisms of the simplest forms of life, so also were included the potentialities which later manifested themselves in the highest forms of psychological activity.

The psyche as the dominant head end of the main axial gradient thus steps into a position of supreme importance. The personality, far from being a matter that can be left out of account in the consideration of a sick individual, may well be not only of great, but perhaps of the greatest importance. It is, to use a crude analogy, the switchboard where all lines meet and hence where, in the organized scheme of the integrated individual, all somatic, so-called organic states reverberate and receive their final direction.

The attempt has been made (Adler) to interpret character traits, particularly as found in the maladaptations of the neuroses and psychoneuroses, by referring them to inferior organs the inefficiency of which in the scheme of the whole individual found expression in the psyche as a feeling of inferiority. This feeling of inferiority caused the individual to avail himself of certain dexterities to compensate for and help to overcome the feeling and these mechanisms, founding in certain organic deficiencies of adjustment, produced the symptoms.

This concept of the psyche, which makes its development contemporaneous and coterminous with the development of the individual as a whole and all-inclusive in its centralized relations with the different parts, makes its inclusion in any study of the individual necessary if that individual is to be really understood and any adequate attempt made to reconstruct in thought the individual from the point of view of the dynamic factors which have produced the end result as we see it in the patient who applies to us for help. Whether the concept of inferior organs is adequate to account for all failures and defects of adjustment is open to serious question. It seems to me to be too anatomical, too static a concept in some particulars, and while inferior organs are undoubtedly at the basis of many grave character defects (cortical inferiority) still, a more dynamic approach is therapeutically frequently more

valuable. In the minor defects of adjustment it seems more useful to see the results as flowing from the bad use to which certain mechanisms have been put in the course of the unfolding personality rather than to see at the basis of such defects an anatomically inferior organ.

The psychoanalysts have long emphasized the conflict between the instinctive tendencies and the aspirations as the focal point about which the symptoms of mental illness revolve. This translation of the psychological symptoms into terms of energy redistribution has been of enormous value in clarifying our thinking about the psychological facts. It remained to correlate the distribution of energy at the psychological level more fully with the energy systems represented by the bodily organs. The organ inferiority concept took the first step in this direction.

The work of the physiologists (Cannon, Crile) and the neurophysiologists (Sherrington) has prepared the way for a still broader concept of the relations between organic states and their psychological repercussions in consciousness. The work on the major emotions (instincts) such as fear, anger, and hunger has shown that in the case of fear, for instance, there are definite physiological conditions incident to the release of adrenalin into the circulation which produces a series of changes, now well known, which register in the psyche as the conscious state of fear. This has brought about a revivification of the James-Lange theory of the peripheral origin of the emotions which has been largely utilized (Kempf) in explaining the organic foundations of character. The primitive emotions correspond to unsatisfied instincts. Hunger, for example, is the instinct to acquire food which, when neutralized, ceases to exist, but when thwarted is a mighty motive for conduct calculated to acquire neutralizing stimuli by bringing about the exposure of certain receptors to food. It is these organic instincts which are the motive forces for conduct and the interference with which, their repression, is registered in the psyche as emotion, which can be further conceived as a motor set of the organism for acquiring certain neutralizing stimuli which, however, does not come to pass.

It is but logical to suppose, and the facts bear out the supposition, that these primitive, phylogenetically old, archaic reaction mechanisms should be served by the oldest parts of the nervous

system, namely, the autonomic or vegetative nervous system, and that the motor sets should be, in the first instance, motor sets of the older variety of muscle, the smooth or involuntary muscle. The instincts are represented, then, by the autonomic apparatus which includes (Kempf) the vegetative nervous system, the smooth musculature, and further the endocrine glands which discharge chemical stimuli into the circulation—the hormones—for bringing about a correlation at this level.

Later in the scheme of development there arises the phylogenetically very much younger portion of the nervous system, the cerebro-spinal nervous system, consisting largely of the neuromuscular apparatus as we ordinarily think of it, that is, in the main, the pyramidal tract system and the voluntary musculature. This apparatus is calculated to bring about, with far greater nicety, the motor responses that so relate the organism with its environment as to make possible the securing of stimuli which will neutralize the instinctive cravings.

The distinguishing features of this more recent development of the nervous system, the cerebro-spinal, are the distance receptors which function as analyzers of the environment and as a result of such analysis condition relatively exact responses to its several characteristics.

Recent studies have indicated (Langelaan, Hunt) that in the striped muscle we have a double system of innervation which so relates the autonomic apparatus and the cerebro-spinal neuromuscular apparatus—the projicient apparatus—as to insure their working in harmony. These studies tend to show that the sarcoplasmatic substance of striped muscle is analogous, if not identical, with the smooth muscle substance, and is innervated by the vegetative nervous system, while the anisotropic disk system is the developmentally more recent portion, and is innervated by the cerebro-spinal nervous system. It can thus come about that the motor sets of the autonomic system can communicate themselves to the voluntary motor apparatus.

The instincts which have at their command the autonomic apparatus and its interoceptors bring about certain motor sets, which are expressed in various forms of visceral and postural tonus. Hunger produces, at this level, the periodic contractions of the

stomach which are registered in the psyche as a desire for food so long as they continue. The projicient apparatus, with the aid of its exteroceptors, can initiate motor responses calculated to expose the stomach receptors to neutralizing stimuli—food—and thus cause the craving to disappear.

Psychology has advanced beyond the purely descriptive stage of development in which it devoted its energies largely to the analysis of the sensory data of experience and was, to that extent, but a refined physiology of the sense organs. It has now become a study of the higher aspects of energy transformation as we see it in the human individual. The great motive forces of conduct lie in the instincts and, instead of seeing sensation as the unit of the psyche, we now realize that it is the registration in consciousness of the unsatisfied instincts which constitute that unit, namely the wish (Holt).

From the point of view of the integrated organism as a whole, its tendencies, the nervous pathways may be considered as the structuralized precipitates of function. That is, functions which, because they have been sufficiently often repeated and because it is essential that they should never fail—like the relation between muscular exertion, respiration, and cardiac rate—come to be laid down in structures which insure certainty and definiteness of response. There remains an unorganized residuum which is capable of reaction with considerable variation to unusual and infrequent forms of stimuli. This unorganized residuum is represented by the wish at the psychic level which has at its disposal both the cerebro-spinal (sensorimotor) and the autonomic apparatus, but it is in the still imperfectly organized region of the latter that the machinery for adjustment to the unusual is contained. Presumably the precipitation of structuralized pathways is still going on.

This approach to the problems of the individual organism, man, considers it as a receiver, transformer, and distributor of energy in which the action patterns are in part laid down in structure, in part represented by physiological functions that take the form of visceral and postural tonicities. The head end of the principal, axial, dynamic gradient is the locus in which is contained the supreme commander of the various mechanisms and structures for translating them into action.

From this point of view it is apparent that the personality, as an energy system, can no longer be neglected in the study of the individual, not only by the psychiatrist, but as well by the internist, if all the factors that enter into a given problem are to be uncovered and the several parts they play adequately evaluated. Like all new concepts, it commends itself as possibly offering explanations for that group of diseases, and those aspects of disease which have, up to the present time, defied explanation.

Certain of the endocrinopathies (particularly thyroid and adrenal) at once suggest this angle of approach as offering problems of adjustment which have as yet not been sufficiently organized to be laid down in structure. Various visceral disorders such as spasms (pylorospasm, spastic constipation) suggest a similar approach in which the spasm can be understood as confining the energy of an organic craving which is unable to gain an outlet in expression by commanding a final, common motor path. This is the physiological mechanism at the basis of what the psychoanalysts call fixation and repression. Some of the myopathies invite study from the point of view of postural tensions. More massive phenomena such as epilepsy and catatonic states come in for like consideration, while in the more obvious functional types of cardiac disorder, the conversions of hysteria and a host of so-called hysterical symptoms, the presence of a psychogenic factor is already accepted. More clearly defined disease types such as diabetes suggest further study along these lines, while such organic conditions as chronic nephritis, pulmonary tuberculosis, and even cancer may have their etiology illuminated by a closer study of the life histories of those in whom they develop, with a view to discovering the dynamic factors which have been at work throughout the life of the individual, and, operating as long-continued stresses, finally broken down the organic compensations in certain directions.

Just as these disease problems can be advantageously approached from this angle, so can other similar problems be perhaps illuminated in the same way. For example, the problem of why certain etiological factors, for instance, the tubercle bacillus, should attack the lung in one person, the kidney in another, etc. The study, for example, of the relation of pulmonary tuberculosis to the shut-in type of character and the dynamic factor back of this character

trait which may well be of more importance than the tubercle bacillus itself, because primary, because offering a point of attack in prophylaxis, and because, unless dealt with, making a cure impossible. It has been in the past usual to explain such problems by heredity, but this stamps the issue as final and irremedial and sterilizes effectually all therapeutic effort.

These lines of research suggest that the question which should be asked of the disordered human machine is, What is the individual trying to do? This question recognizes that the organism is an integrated whole which has a numerous machinery at its command for bringing to pass its aims which are registered in the psyche as desires, wishes. It is in every way quite as appropriate to question the human organism in this way as it is to question a group of such organisms in that integration to which we give the name of nation. We have a right to ask, for example, with what motives the several nations, the United States, England, France, Germany, come to the peace table. Just as the various representations, diplomatic moves, dexterities of the several delegates to the peace conference can only be adequately understood if we know the national motives back of them, so the various disorders of function of the several organs of the individual can only be adequately and fully understood when they are appreciated as parts of the complex mosaic of the individual, as mechanisms which are directed to the larger ends of the individual as a whole.

The discussion of symptoms might be prolonged and the principles herein set forth might be further amplified, particularly along the lines of their application to the interrelations of individuals in the social milieu. Suffice it to rest here with this all too brief setting forth of some of the recent trends which psychiatry has either evolved or taken over and which are suggestive of a time, not far distant, when the personality will receive its due meed of attention in the study of the sick individual, and the internist and the psychopathologist will work hand in hand because of an appreciation of the interdependence of their several problems and the fact that their work is mutually complementary.

Psychiatry, by its unremitting emphasis on the study of the personality make-up, first in disease and later as necessary in order to understand the symptoms of disease when they do develop, has, by

finally pressing physiology into its service, effected a union which for the first time really begins to recognize the importance of considering the individual as a whole. Internal medicine has thought that it was considering the individual as a whole, as a biological unit, when it considered all of the organs and perhaps the most obvious of the personality traits. The study of the personality from the two opposite angles, the psychological and the physiological, has demonstrated the inadequacy of this assumption and indicated quite clearly that between these two lines of approach much more is comprised than we heretofore suspected. Psychiatry, to my mind, is the first medical specialty which at all adequately approaches the problem of the whole individual, and I may say that that statement epitomizes its contribution to general medicine.

THE TOLERANCE OF FRESHLY DELIVERED WOMEN TO EXCESSIVE LOSS OF BLOOD

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SOME years ago I became impressed with the fact that many women may lose considerable quantities of blood during the third stage of labor or shortly thereafter without presenting any of the clinical symptoms which are generally regarded as characteristic of hemorrhage.

In order to test the correctness of my impression, I instructed my assistants to collect and measure the blood lost at that time as a matter of routine in every labor. As the number of observations increased it became desirable to establish a standard for differentiating between physiological bleeding and actual hemorrhage, but upon referring to the standard obstetrical text books and to the monographs upon the third stage of labor, I was surprised by the lack of definite information upon the subject, as well as by the contradictory statements made by the various writers. Thus, in 1886 Barnes said:

"It may be useful to acquire as accurate an idea as possible of what may be considered the natural loss of blood. This standard is very difficult to fix by quantity. Women vary greatly in this respect. Some lose very freely without appearing to be any the worse; whereas others cannot bear the loss of even a moderate amount without exhibiting alarming prostration. When the uterus contracts normally, its substance is compressed, so that the blood in its vessels is squeezed out, much as we squeeze water out of a sponge. The quantity of blood so held in the uterus at the moment of separation of the placenta may be regarded as superfluous *quoad* the wants of the system. It may amount to 1 pound, but it is often less and occasionally more. This I call physiological hemorrhage."

While Barnes's statement is doubtless correct, it is nevertheless too broad to be useful in differentiating or indexing hundreds of observations. Nor are the estimates of other writers more helpful, as one will designate as normal a loss of blood which another would

consider as a serious hemorrhage. The following figures show clearly the varying conceptions of physiological bleeding: Fabre, 80–100 c.c., Tucker, 300 c.c., Champneys, 360 c.c., Commandeur, 500 to 600 c.c., Tarnier and Chantreuil, 600 to 700 c.c., and Ahlfeld, 800 c.c.; while Polak begs the question by stating that hemorrhage did not occur in a series of 1306 consecutive labors. It must be apparent that many of these statements represent merely crude estimates; for, so far as I can gather, only the figures of Tucker and Ahlfeld are based upon actual measurements. Similar variations likewise exist in the notions as to what constitutes actual hemorrhage, its lower limit being placed at 300 and 1000 c.c. by Fabre and Ahlfeld, respectively.

The present study, concerning the amount of blood lost during the third stage of labor and shortly thereafter and its clinical effects, is based upon observations made upon 1000 consecutive spontaneous full-term labors occurring in 1339 obstetrical patients at the Johns Hopkins Hospital (Histories 8161–9500). Of these, 339 histories were not utilized, as they included 162 operative cases, as well as 177 others in which pregnancy had terminated prematurely, or in which the patients left the hospital before delivery.

Our technic for collecting and measuring the blood is as follows: Immediately after the birth of the child a sterile douche pan is placed beneath the buttocks of the patient, where it remains until all bleeding following the birth of the placenta has ceased. After the placenta has been delivered any blood contained within its membranes is allowed to escape into the pan, then poured into a graduate, accurately measured in cubic centimeters, and noted in the history. In this way contamination by amniotic fluid is avoided, and all blood which has escaped during the third stage of labor and after the extrusion of the placenta is collected and measured. This technic is very simple and is preferable to that employed by Tucker and Ahlfeld—the former collecting the blood in a basin held before the external genitalia, and the latter employing a complicated procedure in which the patient's buttocks rest over the mouth of a large copper funnel, which passes through the mattress, the blood being collected in a vessel placed beneath the bed.

Before considering our observations in detail, it seems advisable to say a few words concerning the conduct of the placental period

of labor, as our method differs materially from that employed by Ahlfeld. As is well known, he advocates the greatest possible conservatism, and holds that it results in a diminution in the amount of blood lost, as well as in prompter recovery of the patient. Immediately following the birth of the child, he cuts the cord and leaves the patient absolutely alone for two hours, unless excessive bleeding necessitates prompt expression, or the placenta is extruded spontaneously, the latter occurring in only 13 per cent of his cases. At the end of the period he expresses the placenta by gentle pressure upon the lower abdomen.

I have adopted a different procedure, which is as follows: After the child is born the uterus is gently palpated and the location of its fundus noted, but massage is not employed unless the uterus is boggy in consistency or the bleeding excessive. From time to time the location of the fundus is determined by palpation or inspection, and after the lapse of from five to thirty minutes it is usually noted that it has risen 4 to 6 cm. above its original location, while in some cases an indistinct swelling has likewise appeared just over the symphysis. This indicates that the placenta has become separated from its attachment, has been extruded from the uterine cavity, and lies free in the lower uterine segment or upper part of the vagina. As Ahlfeld's observations have taught us that in seven cases out of eight the placenta will remain in this location until expressed by pressure from above, I have been unable to convince myself that there is any advantage in waiting a specified length of time before expressing it; and consequently, as soon as the rising of the fundus indicates that it has been extruded from the uterine cavity, I express it from the vagina by gentle pressure upon the fundus. On the other hand, I believe that routine massage of the uterus only tends to disturb and prolong the process of separation, and should, therefore, be avoided; while premature attempts to express the unseparated placenta by the original Credé method frequently lead to retention of placental fragments and thus greatly increase the amount of bleeding and the frequency of radical intervention. Consequently, I employ the typical Credé method of expression with the greatest circumspection, and only in the presence of serious bleeding, or after spontaneous separation of the placenta has failed to occur within one hour after the birth of the child.

The following figures give a clear idea of our conduct of the third stage, which is apparently justified by the results, to which reference will later be made.

	Cases
Placenta born spontaneously	9
Placenta expressed from vagina	973
Placenta expressed by typical Credé	18
Placenta removed manually	0
	1000

In the entire series, the average time elapsing between the birth of the child and the extrusion of the placenta was 15.3 minutes, the extremes being spontaneous expulsion immediately following the birth of the child and a difficult Credé expression at the end of ninety minutes.

In Chart I is given a graphic representation of the duration of the placental period in our series of cases, and shows that the most frequent time for delivery of the placenta is between ten and fifteen minutes after the birth of the child, or somewhat less than the arithmetic average.

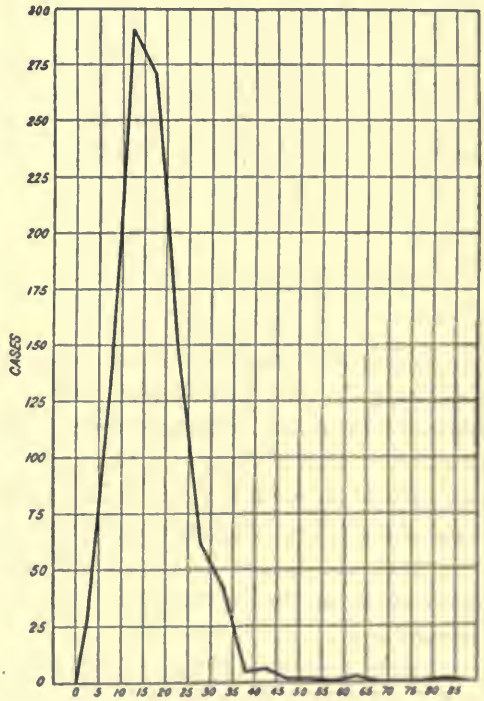

CHART I. SHOWING DURATION OF PLACENTAL PERIOD IN 1000 CONSECUTIVE SPONTANEOUS LABORS.

Upon analyzing the amount of blood lost in our series of 1000 spontaneous labors, we find that the average bleeding was 343.7 c.c., with the extremes varying from zero to 2400 c.c., the placental period having been entirely bloodless in two patients. Table I gives the incidence of the varying loss of blood:

TABLE I

SHOWING THE VARYING AMOUNT OF BLEEDING IN 1000 SPONTANEOUS LABORS

QUANTITY OF BLOOD LOST, C.C.	CASES
0	2
1– 99	88
100– 199	210
200– 299	227
300– 399	148
400– 499	120
500– 599	75
600– 699	31
700– 799	28
800– 899	15
900– 999	7
1000–1099	8
1100–1199	7
1200–1299	8
1300–1399	4
1400–1499	4
1500–1749	4
1750–1999	—
2000–2249	3
2250–2499	1
Average 343.7 c.c.	1000

It must not be understood, however, that this average loss gives a correct idea concerning the amount of bleeding which one is most likely to encounter in spontaneous labor, as that amounted to less than 300 c.c. in 527 out of 1000 cases. This is still further accentuated by Chart II, which graphically illustrates the conditions in our 1000 cases, and shows that the most usual loss varies between 100 and 300 c.c., and that the higher average for the series has resulted from the inclusion of the relatively rare cases of profuse hemorrhage.

These figures correspond approximately with those of Tucker and Champneys (300 to 360 c.c.), and are much smaller than those given by Commandeur, Tarnier and Chantreuil, and Ahlfeld (500–800 c.c.). In the last 2058 cases studied by Ahlfeld the average loss was 505.1 c.c., which is 161.4 c.c., or one-third, greater than in our series. Whether this is fairly attributable to the difference in our management of the placental period, I hesitate to state; but in any event it can scarcely serve as an argument in support of the

view that extreme conservatism necessarily leads to a pronounced diminution in the amount of bleeding.

While such statistics may be of practical value to the obstetrician, they are of little interest to medical men in general; but, on the other hand, our observations as to the incidence of actual hemorrhage, and more particularly concerning the tolerance which freshly delivered women appear to exhibit to it, are of general significance. Upon entirely arbitrary grounds I selected 600 c.c. as the limit between physiological bleeding and post-partum hemorrhage, and our figures show that 130 cases in the series (13 per cent) belong in the latter category. Table II shows the frequency and amount of such hemorrhages:

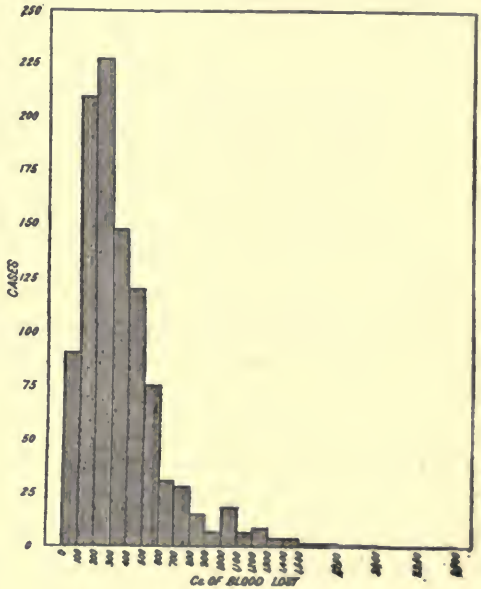

CHART II. SHOWING AMOUNT AND FREQUENCY OF BLEEDING FOLLOWING 1000 CONSECUTIVE SPONTANEOUS LABORS.

TABLE II

SHOWING FREQUENCY AND AMOUNT OF POST-PARTUM HEMORRHAGES IN 1000 SPONTANEOUS LABORS

QUANTITY OF BLOOD LOST, C.C.	CASES
600	130
800	71
1000	49
1250	18
1500	8
2000	4
2400	1

As experience has taught me that in normal freshly delivered women serious symptoms do not follow hemorrhages of less than 1000 c.c., our interest is centered upon the 49 women who lost one liter or more. Of these, 31 lost between 1000 and 1250 c.c. of blood

and 18 more than that quantity. As only one patient in the first group presented symptoms of acute anemia, we are particularly interested in the 18 women of the second group, abstracts of whose histories are given at the end of the article. Of these, 10 lost less and 8 more than 1500 c.c. of blood, the latter being distributed as follows:

2 patients lost 1500 c.c. (Cases XLII and XLIII)
1 patient lost 1600 c.c. (Case XLIV)
1 patient lost 1700 c.c. (Case XLV)
2 patients lost 2000 c.c. (Cases XLVI and XLVII)
1 patient lost 2100 c.c. (Case XLVIII)
1 patient lost 2400 c.c. (Case XLIX)

While 49 hemorrhage cases, in which the loss of blood was 1000 c.c. or more, constitute too small a number to justify the formulation of far-reaching conclusions, I nevertheless believe that their study will bring out several points of interest and importance. The only other study of the kind with which I am familiar was made in 1904 by Ahlfeld, who reported that in a series of 6000 labors, post-partum hemorrhages amounting to 1500 c.c. or more occurred in 159 women, an incidence of 2.65 per cent as compared with our 0.8 per cent. His cases were divided as follows:

132 patients lost 1500–2000 c.c.
23 patients lost 2000–2500 c.c.
4 patients lost 2500 c.c. or more,

with 4 deaths in the first group, 1 in the second, and none in the third. Furthermore, he related the history of a patient not included in his series who recovered from a hemorrhage of 3250 c.c. without serious symptoms.

It is generally believed that patients suffering from serious hemorrhage present a succession of more or less characteristic clinical symptoms, the most important of which are: rapid and small pulse, shock, air hunger, and, if recovery ensues, a rapid decrease in the percentage of hemoglobin, together with a marked diminution in the number of red cells, which reaches its lowest point by the third day, and then gradually returns to normal. The histories given below, however, conclusively demonstrate that not a few freshly

delivered women may lose excessive quantities of blood without presenting any evidence of shock, and that occasionally the extent of the hemorrhage would not have been appreciated had the blood lost not been collected and measured. Thus, only 1 of the 31 women who lost between 1000 and 1250 c.c. presented any immediate symptoms attributable to loss of blood, but she was considerably shocked, and had a pulse rate of 118 one hour and a quarter after delivery (Case XXX). Furthermore, only 4 of the 18 patients losing from 1250 to 2400 c.c. caused us any anxiety; none was seriously ill and all recovered.

It is currently believed that the pulse is unusually slow during the normal puerperium, and that the readiest method of evaluating the effect of hemorrhage is by its increased rate and poor quality. Our observations, however, show that the first assumption is incorrect, and that in freshly delivered women the second does not occur with the regularity one might expect.

In going over our 1000 cases, particular attention was directed to the condition of the pulse during the forty-eight hours following delivery, and, as it was counted as a matter of routine at four-hour intervals, we usually had a record of twelve counts for the period. The highest count in each case was recorded and used for statistical study, and the following table shows that most of the women at some time during this period had a more rapid pulse rate than is generally believed.

TABLE III

SHOWING THE HIGHEST PULSE RATE DURING THE FIRST FORTY-EIGHT HOURS OF THE PUERPERIUM

PULSE BELOW	CASES WITHOUT HEMORRHAGE	CASES WITH HEMORRHAGE	TOTAL
60	1	—	1
60– 69	15	1	16
70– 79	97	7	104
80– 89	273	31	304
90– 99	314	44	358
100–109	112	25	137
110–119	36	14	50
120–129	17	5	22
130 and over	7	1	8
	872	128	1000

In the two groups the average rate was 91.66 and 96.45 respectively, which apparently indicates that the average effect of hemorrhage is to raise the pulse rate by only five beats. Chart III represents these figures graphically, and clearly shows that the pulse rate most usually encountered is between 80 and 100, irrespective of whether labor is followed by physiological bleeding or by actual hemorrhage.

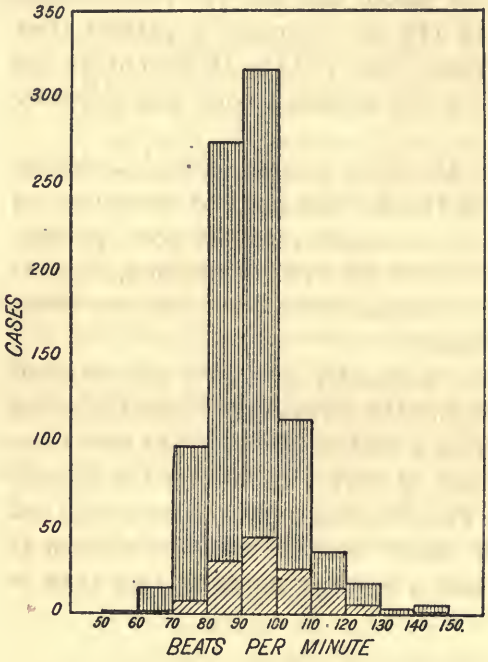

CHART III. SHOWING HIGHEST PULSE RATE DURING THE FIRST 48 HOURS FOLLOWING DELIVERY IN 1000 SPONTANEOUS LABORS. VERTICAL AND OBLIQUE LINING INDICATES CASES WITH OR WITHOUT HEMORRHAGE, RESPECTIVELY.

Furthermore, it is interesting to compare these findings with those observed in the operative deliveries, which were interpolated between the 1000 normal labors. Of the 162 operations, 138 were not associated with hemorrhage, and these showed an average pulse rate of 101.9, which in turn was five beats higher than that observed in the spontaneous labors followed by hemorrhage.

From a study of these figures it seems justifiable to conclude: (1) That the pulse rate following normal spontaneous labor is higher than is generally believed; (2) that post-partum hemorrhage leads to a slighter relative elevation than would be anticipated *a priori;* and (3) that the strain of a difficult labor which necessitates operative termination results in a greater average elevation than does post-partum hemorrhage.

Professor Raymond Pearl was kind enough to study these figures from a statistical point of view, and has formulated his data in Table IV:

TABLE IV

PULSE RATE IN SPONTANEOUS AND OPERATIVE LABORS

	SPONTANEOUS LABORS		OPERATIVE LABORS
	WITHOUT HEMORRHAGE	WITH HEMORRAHGE	WITH HEMORRHAGE
Average	91·66± ·27	96·45± ·75	101·89± ·91
Standard Deviation	11·90± ·19	12·61± ·53	15·81± ·64
Coefficient of variation	12·98± ·21	13·07± ·56	15·52± ·64
Mode	88·48±1·36	93·08±1·30	91·72±1·53
Median	91·09	95·18	98·59
Skewness	+ ·27± ·11	+ ·27± ·08	+ ·64± ·12

from which he has drawn the following conclusions:

"1. In spontaneous labors the average pulse rate is increased only about five beats in the cases with hemorrhage as compared with those without. This increase, while absolutely small, is clearly significant statistically, having regard to the probable errors. In operative labors the rate is about ten beats higher, without hemorrhage.

"2. The modal pulse rate is smaller than the average in every case; the skewness of the distribution being in the positive direction.

"3. In the case of spontaneous labors the skewness is not certainly significant in comparison with its probable error."

Passing from these general statistical data to the condition of the pulse in the individual cases of severe hemorrhage, I find it impossible to make any categorical statement concerning it, and I can only say that in many cases its rate and character during or shortly after post-partum hemorrhage in no way correspond to the quantity of blood lost, and, therefore, they are not necessarily indicative of the gravity of the condition. Table V gives a graphic idea of such variations.

From these figures it is clearly evident that in certain cases the immediate clinical symptoms were not proportionate to the degree of hemorrhage, and in several instances, notably in Case XLVIII, the extent of hemorrhage would have escaped observation had the blood lost not been measured as a routine procedure. Likewise, in Case XLIX, the pulse rate and the general condition of the patient gave no indication that 2400 c.c. of blood had been lost; although the fall of the blood pressure to 70 immediately after its cessation indicated profound shock, and the decrease in the hemoglobin con-

tent to 38 per cent on the third day gave conclusive evidence of the existence of pronounced anemia.

TABLE V

SHOWING PULSE RATE IMMEDIATELY AFTER, AND HEMOGLOBIN PERCENTAGE THREE DAYS AFTER POST-PARTUM HEMORRHAGE

CASES	AMOUNT BLEEDING	PULSE	HEMOGLOBIN THIRD DAY, PER CENT	NOTES
30	1000 c.c.	118	?	Definite shock.
42	1500 c.c.	136	?	Pulse 84 four hours later.
43	1500 c.c.	90	55	No immediate symptoms.
44	1600 c.c.	rapid	42	Pulse 75 four hours later.
45	1700 c.c.	good	?	Pulse 65 four hours later.
46	2000 c.c.	good	38	Pulse 104 one and a half hours later (red cells fifth day, 2,632,000).
47	2000 c.c.	good	42	Pulse 78 three hours post-partum.
48	2100 c.c.	84	40	Pulse 104 one hour later.
49	2400 c.c.	100	38	Pulse 115 one and a half hours later (blood pressure 70 immediately after).

Table V also gives information concerning the hemoglobin content of the blood on the third day, and makes it apparent that in five of the severe cases a pronounced reduction had occurred. In several instances a rapid return to normal was noted, but in others the low percentage persisted throughout the patient's stay in the hospital.

Unfortunately, routine hemoglobin examinations were not made in all of the patients losing 1000 c.c. or more of blood, but, as far as our figures go, it may be said that the hemoglobin content was not markedly lowered unless the hemorrhage exceeded 1250 c.c., but beyond that limit several marked reductions were noted. For example, readings of 40 per cent were made upon two patients who lost 1350 and 1400 c.c. respectively, which are practically identical with those noted in patients losing from 2000 to 2400 c.c.

It is apparent that a certain proportion of freshly delivered women may lose from 1250 to 2400 c.c. of blood with comparative impunity, and present such slight immediate symptoms that the extent of hemorrhage might escape recognition if the blood were not collected and measured. If the usual computation be accepted, that the total amount of blood in the body corresponds to 1/13 of the body weight, and assuming that the latter averages 130 pounds, such hemorrhages mean that the patients had lost from one-quarter

to one-half of their total blood. In males and non-pregnant women such a loss would inevitably be followed by alarming symptoms of shock and acute anemia, yet the patients here mentioned did not so suffer, nor was their general condition so serious that the necessity for transfusion was at any time entertained.

The question accordingly arises as to how such an immunity is brought about, and why the characteristic symptoms of shock do not always develop. There can be no question concerning the actuality of the hemorrhage, as its amount was accurately measured, and furthermore, the striking reduction in the hemoglobin content on the third day, as well as the marked pallor and definitely anemic appearance of some of the patients, affords still further evidence of a serious loss of blood. Yet in many cases the pulse remained good in quality and was scarcely accelerated in rate.

The first explanation to occur to one is that so decided an increase in the total amount of blood had taken place during the latter months of pregnancy that the amount lost by hemorrhage represented a smaller proportion of the total content in pregnant women than would have been the case in non-pregnant individuals, with the result that the fraction remaining in the body is sufficient to tide over the immediate needs. A certain plausibility is lent to such an explanation by the observations of Miller, Keith, and Rountree, made in my service, that an increase in the total amount of blood actually occurs during pregnancy. I do not believe, however, that such an explanation is permissible, for two reasons: First, because the normal increase is only slight; and secondly, that the low hemoglobin content noted after the serious hemorrhages affords indubitable evidence that a large proportion of the blood in the body had actually been lost.

Some other explanation for the relative immunity must, therefore, be invoked; but, unfortunately, we are not in a position to do so satisfactorily. I am inclined, however, to believe that it is in some way associated with other protective processes, which develop during the last weeks of pregnancy and at the time of labor. Slemons has clearly shown that the nitrogenous metabolism at the time of labor is reduced to a minimum, while my own unpublished observations upon the respiratory exchanges indicate that the parturient woman can go through labor with little or no increase in energy

consumption, as indicated by the oxygen intake and carbon dioxide output. In other words, as I loosely express it to the students, she is conducting her body upon a "low gear" metabolism, so that the amount of energy necessary for the demands of the body plus the increased work incident to labor is scarcely increased.

If this supposition is correct, it may be permissible to assume that the temporary immunity to excessive loss of blood may in some way be connected with such a mechanism, and that the relative absence of shock may be due to the fact that for a few hours after labor the patient can get along upon a greatly diminished amount of blood, so that by the time the normal metabolism has been re-established, the reparative processes will be sufficiently well under way to tide the woman over the immediate emergency. It must, however, be understood that such an explanation is entirely theoretical and is not supported by any known facts.

Finally, in order to avoid any possibility of misunderstanding, I wish to emphasize strongly that I do not claim that freshly delivered women are entirely immune to excessive hemorrhage, as to do so would be running contrary to ordinary clinical experience. But what I wish to point out is that many women may lose large quantities of blood with apparent impunity, and that routine measurement will show that an excessive loss occurs much more frequently than is generally believed. In my experience the average normal women can lose 1250–1500 c.c. of blood with little or no ill effect; and many can lose much larger quantities with relative impunity. At the same time a recent observation in private practice has taught me that a loss of 1800 c.c. may put the life of the patient in the greatest jeopardy, and Ahlfeld has reported several fatalities in which the loss barely exceeded 1500 c.c.

Abstract of histories of patients losing 1250 c.c. or more blood (including one patient presenting symptoms following a loss of only 1000 c.c.).

(In Cases I to XXIX, the loss varied from 1000 to less than 1250 c.c.)

Case XXX. 1000 c.c. History 8210, due to partial separation of placenta, sixteen years old, I para. Pelvis normal, L. O. P. Prolonged second stage. Profuse bleeding immediately following birth of the child necessitating expression by Credé in four minutes. Patient evidently shocked; pulse 118 $1^{1}/_{4}$ hours post-partum.

CASE XXXI. 1250 c.c. History 8300, due to uterine atony. Twenty-three years old, I para. Pelvis normal, L. O. A., labor easy. Bleeding after expulsion of placenta from vagina. No note as to symptoms. Pulse 104 two hours post-partum.

Case XXXII. 1250 c.c. History 9286, due to uterine atony. Twenty-three years old, I para. Pelvis normal, R.O.A. Pre-eclamptic toxemia treated for three weeks before labor. Labor prolonged, second stage four hours thirteen minutes, bleeding entirely after expression of placenta from vagina. No symptoms. Pulse 84 three hours post-partum.

Case XXXIII. 1275 c.c. History 8782, due to uterine atony. Seventeen years old, I para. Pelvis slightly generally contracted, L. O. A., labor easy. Bleeding after expulsion of placenta. Condition at all times good. Pulse 75 $1^3/_4$ hours post-partum.

CASE XXXIV. 1300 c.c. History 8491, due to uterine atony. Twenty years old, I para. Pelvis normal, L. O. A., labor prolonged, second stage three hours. Bleeding after expression of placenta lasting for twenty minutes. Although the patient was pale for two days, the pulse rose only to 96 immediately after the bleeding and soon returned to normal.

CASE XXXV. 1350 c.c. History 8310, due to partial separation of placenta. Twenty years old, I para. Pelvis normal, R. O. A. Labor easy, repeated attempts to express placenta by Credé were not successful until one hour and twenty minutes after delivery. During the entire period bleeding at intervals, which ceased completely after expression. Condition good, pulse 95 $1^1/_2$ hours post-partum.

CASE XXXVI. 1350 c.c. History 9492, due to uterine atony. Twenty-four years old, I para. Pelvis normal, L. O. A., labor easy. Bleeding entirely after expression of placenta, uterus boggy. Patient in excellent condition at end. Pulse 88 two hours post-partum. Hemoglobin: second day 55 per cent; fourth day 40 per cent; eighth day 55 per cent.

CASE XXXVII. 1375 c.c. History 9494, due to uterine atony. Twenty-two years old, I para. Pelvis normal, L. O. A., labor easy. Bleeding after completion of third stage. Patient in excellent condition. Pulse 104 two hours post-partum. Hemoglobin: second day 70 per cent; fourth day 55 per cent; tenth day 65 per cent.

CASE XXXVIII. 1400 c.c. History 8446, due to uterine atony. Twenty-five years old, I para. Pelvis slightly generally contracted, R. O. A., labor normal. Bleeding after expression of placenta from vagina. No symptoms. Pulse 80. Hemoglobin on fourth day 55 per cent.

CASE XXXIX. 1400 c.c. History 8494, due to uterine atony. Twenty-four years old, I para. Pelvis normal, L. O. A., labor easy, bleeding throughout the third stage, but particularly after expulsion of placenta. Vigorous

massage necessary for one hour afterwards. Pulse 90. Hemoglobin: 55, 40 and 60 per cent; immediately post-partum, third and tenth days respectively.

CASE XL. 1450 c.c. History 9105, due to partial separation and atony. Seventeen years old, I para. Pelvis generally contracted rachitic. L. O. T., labor prolonged, $31^3/_4$ hours. Bleeding began immediately after the birth of the child; expression by Credé eighteen minutes later. Patient's condition always good. Pulse 98 $2^1/_2$ hours post-partum; $1^1/_2$ hours before birth of the child blood pressure was 124/94, while one hour after the birth of the child it had fallen to 98/74. Hemoglobin: $1^1/_2$ hours a. p. 94.6; one hour p. p. 89 per cent; third day 67.3 per cent; tenth day 90 per cent.

CASE XLI. 1475 c.c. History 9073, due to uterine atony. Eighteen years old, II para. Pelvis normal. L. O. A., labor easy. Bleeding following expression of placenta from vagina. The condition was never alarming and the amount of bleeding would not have been noted had the blood not been measured. Blood pressure on admission 138/80; after conclusion of hemorrhage 98/54. Except for this no symptoms. Hemoglobin: end of second stage 82.6 per cent; one hour p.p. 81.4 per cent; third day 54.5 per cent; tenth day 66.8 per cent.

CASE XLII. 1500 c.c. History 8804, due to partial separation of placenta and uterine atony. Eighteen years old, I para. Pelvis normal, L. O. A., labor easy. Bleeding commenced immediately after the birth of the child, necessitating Credé's method. It continued afterwards and gradually ceased after the hypodermic administration of pituitrin. Although the pulse rose immediately thereafter to 136, patient's condition was never alarming; pulse fell to 85 four hours later and did not exceed 104 afterwards.

CASE XLIII. 1500 c.c. History 8904, due to partial separation of placenta. Twenty-four years old, I para. Pelvis normal, R. O. A., labor easy. Oozing throughout entire third stage ceasing immediately afterwards. No symptoms. Pulse 90. Hemoglobin immediately p.p. 65 per cent; third day 55 per cent and twelfth day 60 per cent.

CASE XLIV. 1600 c.c. History 8835, due to uterine atony. Nineteen years old, II para. Pelvis normal, L. O. A., labor easy. Bleeding after extrusion of placenta. Immediately thereafter pulse was rapid, but never thready. Four hours later it fell to 75. Hemoglobin only determined on ninth day, when it was 42 per cent.

CASE XLV. 1700 c.c. History 9356, due to uterine atony. Thirty-nine years old, V para. Pelvis normal, R. O. P., prolonged labor. Hydramnios, 3 liters. Bleeding after completion of third stage. Retention of succenturiate lobe was suspected but was not found on introducing hand *in utero*.

Bleeding stopped after a hot intra-uterine douche. Pulse "good quality," 60 twelve hours p.p.

CASE XLVI. 2000 c.c. History 8268, due to uterine atony. Twenty-three years old, I para. Generally contracted funnel pelvis. L. O. A., labor easy. Bleeding began immediately after birth of the child and as it continued after the expulsion of the placenta the cervix was examined and found not to be torn, whereupon the hand was introduced into the uterus and found a few shreds of membranes but no placental tissue. Hemorrhage controlled by intra-uterine pack. The patient was not sufficiently shocked to cause a special note to be made in the history; $2^1/_2$ hours later pulse 104. Hemoglobin: second day 38 per cent; fifth day 39 per cent; sixteenth day 38 per cent; the number of red cells varying from 3,120,000 to 2,632,000 to 2,832,000 on the respective days.

CASE XLVII. 2000 c.c. History 8393, due to retained fragments of placenta. Twenty-eight years old, V para. Pelvis normal, R. O. P., labor rapid. Bleeding following expulsion of placenta was checked only after manual removal of the retained fragments followed by hot intra-uterine douche. Condition at no time alarming. Pulse 78 three hours p.p. Hemoglobin immediately after bleeding 60 per cent; first day 42 per cent; eleventh day post-partum 42 per cent.

CASE XLVIII. 2100 c.c. History 9265, due to partial separation of placenta. Twenty-nine years old, III para. Pelvis normal, L. O. P. Slightly prolonged labor. Bleeding began ten minutes after the birth of the child and continued until the placenta was expressed from the vagina thirty minutes later. During this entire period the uterus remained firm and the loss of blood would not have been noticed had it not been collected and measured. No treatment required. Pulse of good quality 84, one hour later 104. Hemoglobin: twenty-four hours p.p. 40 per cent; fourth day 42 per cent.

CASE XLIX. 2400 c.c. History 8941, due to retention of placental cotyledon. Thirty-two years old, I para. Pelvis normal, L. O. A., labor easy and rapid. Bleeding during and after the third stage necessitating introduction of the hand *in utero* and the removal of a retained cotyledon. Immediately thereafter the pulse was 100 and the blood pressure 70; $1^1/_2$ hours later the pulse had risen to 115, where it remained for the next twenty-four hours. Hemoglobin immediately post-partum 50 per cent; second day 38 per cent; and tenth day 60 per cent.

BIBLIOGRAPHY

Ahlfeld, "Die Blutung bei der Geburt und ihre Folgen für die Frau," *Ztschr. f. Geburtsh. u. Gynäk.*, 1904, LI, 341–364.

Barnes, "Post-partum Hemorrhage." "Lectures on Obstetrical Operations," IV ed., 1886, 440–465.

Champneys, "Mechanism of the Third Stage of Labor," II. *Tr. Obst. Soc., Lond.*, 1887, XXIX, 166.

Commandeur, "Perte sanguine après la deliverance. Bar, Brindeau et Chamberlent—La pratique de l'art des accouchements," 1914, I, 453–455.

Fabre, "Précis d'obstetrique," 1910, 366.

Miller, Keith, and Rountree, "Plasma and Blood Volume in Pregnancy," *J. Am. M. Ass.*, 1915, LXV, 779–782.

Polak, "A Study of the Management of the Placental Stage of Labor," *Surg., Gynec. & Obst.*, 1915, XXI, 590–593.

Slemons, "Metabolism during Pregnancy, Labor, and the Puerperium," *Johns Hopkins Hosp. Rep.*, 1904, XIII, 111.

Tarnier et Chantreuil, "Traité de l'art des accouchements," 1888, I, 744.

Tucker, "Birth of the Secundines," *Am. Gynæc. & Obst. J.*, 1898, XII, 569–593, 767–794.

INTRATRACHEAL PULMONARY IRRIGATION

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THE studies which are to be included in this report were incited primarily by the hope that the intratracheal route might be utilized in the more direct application of therapeutic agents in pulmonary inflammatory conditions. While the main objective has not been attained, the preliminary experiments have been extensive and have yielded results which in themselves seem worthy of record.

Contrary to general opinion, the lungs are by no means as susceptible to the introduction of foreign material as is generally assumed. Huge quantities of fluid can be introduced through the trachea without any untoward results. This has led to the analysis of the rôle that fluid within the pulmonary alveoli may play, and it is evident, firstly, that the significance of pulmonary edema as a cause of death is challenged, and secondly, that in acute inflammatory processes, fluid in the pulmonary parenchyma may be a means of disseminating the infection through the lung tissue. These preliminary studies will be reported in the order indicated above, and will then be followed by a discussion of the possible utility of the intratracheal route in the application of therapeutic agents to pulmonary lesions.

Material and Method. All of the experimental work has been done upon normal dogs, and the material has been brought into the lungs by the usual method of intratracheal insufflation. The technic is very simple and involves no complicated apparatus. A rubber tube of about 8 mm. in diameter, and with a heavy wall which provides the desired rigidity, is passed into a glass tube with a lumen slightly larger than the diameter of the rubber cannula. It is necessary to have the glass tubing of heavy wall to avoid the danger of breakage, and it can be most conveniently manipulated if it is about 20 to 24 cm. in length. After sterilization the glass

tube is introduced through the mouth of the animal until its end is within the opening of the trachea. During this manipulation the rubber cannula is withdrawn about 2 cm. from the end of the glass tube, so that it does not come into contact with the saliva and thus become contaminated. Very gentle pressure exerted upon the rubber tubing that projects from the proximal end of the glass protecting tube is sufficient to force the rubber cannula down through the trachea. The glass tube thus serves two purposes —it avoids the necessity of directing the cannula into the trachea with the hand, which obscures the vision, and it also permits the passage of the cannula into the trachea without danger of contamination. That the cannula is in the trachea can be readily determined, for after it has been passed in for a certain distance, that is, as far as the bifurcation, its path becomes obstructed. This is not the case when it is entering the stomach. Such manipulation can be done much more readily if the animal is thoroughly anesthetized.

For the introduction of fluid two methods have been employed, the method of choice depending largely upon the amount of fluid to be introduced. With amounts up to 50 c.c., satisfactory results have been secured by simply connecting the pipette containing the fluid with the projecting end of the cannula, and forcing the fluid in by means of a compression bulb attached to the other end of the pipette. With such small amounts, where it is essential that the material be introduced quantitatively, this method has invariably been employed, for if air is forced through the cannula after the introduction of the fluid, there is no danger of loss. With larger amounts, where a slight loss does not cause an appreciable error or where the material is to be introduced for a long time, the gravity method has been used. In such a case the cannula is connected by rubber or glass tubing with an elevated reservoir, from which the flow of fluid is regulated by a pinch-cock.

Tolerance of the Lung for Fluid Introduced through the Trachea. Although studies on the production of pneumonia by intratracheal insufflation, which have been carried on so extensively in the past ten years, indicate that a considerable quantity of material may be introduced into the pulmonary parenchyma by this route, recent experiments by Wollstein and Meltzer (1) indicate that in one animal at least (a dog), death resulted after the introduction of 60 c.c. of fluid, and in the opinion of the authors it was brought about by drowning. This result is quite contrary to the experiences to be quoted below.

A series of experiments was undertaken with the intention of determining how much fluid can be introduced into the lung through the trachea with safety. Salt solution was insufflated in definite amounts per kilogram of body weight. Five cubic centimeters were readily tolerated and the quantity was increased to 20 c.c. per kilogram of body weight. At this point it became evident that 20 c.c. approached the limit that could be introduced, not because of any evident harmful effect upon the animal, but simply because the capacity of the lungs had been reached. When 30 c.c. per kilogram of body weight was attempted, before the amount was completely introduced there was a flow of fluid back through the trachea and mouth. In fact, not in every case could 20 c.c. per kilogram be introduced without refluence of some of the salt solution. It should be noted that 20 c.c. of salt solution per kilogram of body weight in the animals which were utilized amounted to between 200 and 450 c.c. in total volume.

The protocol given herewith is that for dog Pn-37, the animal mentioned above as having received an insufflation of 30 c.c. per kilogram of body weight. It is typical of the animals of this series.

Pn-37. April 9, 1918, 4:25 P.M. Intratracheal insufflation of 393 c.c. of physiological salt solution (30 c.c. per kilogram). After about 275 c.c. had been introduced the excess was expelled. The dog was removed from table immediately and allowed to recover from the anesthesia. During this time some of the fluid escaped from the mouth. There was no manifest distress aside from an occasional cough.

April 10, 1918. The dog appeared perfectly normal and was killed with chloroform. Some fluid not yet absorbed remained in the lung. The surface of the lower right lobe was somewhat mottled and brownish red. The other lobes appeared normal. On section the lungs showed nothing abnormal.

Microscopically: There was slight hemorrhage into the bronchi, with an occasional polymorphonuclear leucocyte and slight mechanical disturbance of the alveoli as evidenced by their variation in size. There was no evidence of fluid or extensive damage. The presence of polymorphonuclear cells within the alveolar walls and a few in the lumen of the alveolus showed that there had been a slight, but definite, inflammatory reaction.

This protocol, which is typical of a large series, indicated beyond peradventure that the lung will tolerate its capacity of fluid intro-

duced by the intratracheal route, and that under the conditions of the experiment there is absolutely no danger of "drowning" the animal.

The question now arises whether the fluid actually enters the alveoli of the lung, or whether it simply runs into the ramifications of the tracheal tree and becomes refluent before the alveoli are reached. It is quite obvious that the amount of fluid that can be introduced (200 to 400 c.c.) could not be confined to the trachea and bronchi, but in order to make the evidence absolute, the last portion of fluid injected, perhaps 25 c.c., was stained with India ink and the animal immediately sacrificed. The ink penetrated and not only stained the lower lobes of the lung throughout, but it was found in widely distributed patches in the upper lobes. None of the lobes was free from the discoloration.

These experiments indicate clearly that fluid introduced into the trachea will find its way into the alveoli themselves and that the pulmonary parenchyma can be filled to capacity with normal salt solution without provoking any untoward symptoms in the subject of the experiment.

Absorption from the Lung. It becomes necessary now to determine the fate of the fluid which is left in the lung following the insufflation. The absorptive powers of the lung have not been determined to any extent, but it has always been believed that the very extensive blood and lymph vascular supply in this tissue can care for a relatively large amount of material. That this is true is quite evident from experiments in which phenolsulphonephthalein was utilized as an indicator. In the same subject the excretion of this dye by the kidneys was determined after intravenous, intramuscular, and intrapulmonary injections. Of course, a definite period was allowed to elapse between the determinations of the excretion of the drug after its introduction by the different routes.

The amount of the phenolsulphonephthalein introduced has always been the same, 6 mg., although in the case of the intratracheal insufflations this quantity was contained in 15 c.c. The volume of the intramuscular and intravenous injections was 1 c.c. The elimination was measured in dogs anesthetized with ether. Before the injection of the drug the dogs were given 250 c.c. of water by stomach and a catheter was passed into the bladder. After the injection or insufflation of the phenolsulphonephthalein

solution the contents of the bladder were removed and tested every five minutes until excretion of the drug was detected.

In addition to the tests for the time of appearance of the phthalein, the urinary excretion for half-hourly periods was collected separately, the bladder being washed out at the end of every such period, and each specimen was tested for its phthalein content. Such collections were made up to two hours after the introduction of the drug.

Pn-87. June 28, 1918. 250 c.c. water into stomach at 10.39 A.M.; 6 mg. phthalein (in 15 c.c.) into lung at 10.42 A.M. The drug first appeared in the urine at 10.55 A.M. (thirteen minutes). Urine excreted collected in half-hourly periods.

Titrations:	Per Cent
First half hour	12.5
Second half hour	20.0
Third half hour	16.6
Fourth half hour	8.0
(2 hours)	57.1

July 15, 1918. 250 c.c. water into stomach at 2.37 P.M.; 6 mg. phthalein injected intramuscularly at 2.39 P.M. The drug first appeared in the urine at 2.54 P.M. (fifteen minutes). Urine excreted collected in half-hourly periods.

Titrations:	Per Cent
First half hour	5.5
Second half hour	26.0
Third half hour	17.0
Fourth half hour	24.0
(2 hours)	72.5

July 16, 1918. 250 c.c. water into stomach at 9.58 A.M.; 6 mg. phthalein into jugular vein at 10.17 A.M. First appearance of the drug at 10.22 A.M. (five minutes). Urine collected at half-hourly periods.

Titrations:	Per Cent
First half hour	24.0
Second half hour	36.4
Third half hour	10.5
Fourth half hour	7.25
(2 hours)	78.15

A tabulation of these results, arranging the values in parallel series, shows:

	Intrapulmonar	Intramuscular	Intravenous
First positive	13 min.	15 min.	5 min.
First half hour	12·5%	5·5%	24·0%
Second half hour	20·0	26·0	36·4
Third half hour	16·6	17·0	10·5
Fourth half hour	8·0	24·0	7·2
Totals	57·1	72·5	78·1

This experiment, valuable as it may be to indicate the absorption of a small amount of fluid through the tissues of the lung, does not give any indication of the rapidity of the absorption and restitution to normal of the pulmonary parenchyma when it is filled to capacity. To arrive at some conclusion in this association, a series of experiments were conducted in which the animals were sacrificed at varying intervals after the pulmonary insufflation to determine the residual fluid in the lung tissue.

Dogs Pn-50 to Pn-55 were each given 20 c.c. of salt solution per kilogram of body weight. After varying intervals they were killed and the lungs were examined. As before, no disturbance was noted in the general condition of the animals immediately after the insufflation or during the period of observation. The protocols for some of these dogs follow.

Pn–50. Received 220 c.c. of salt solution and was killed within five minutes of the completion of the insufflation. The lungs, aside from a small portion of the margin of the upper lobes, were found to be completely filled and distended with fluid. In fact, it is difficult to fill the lungs to such an extent that the upper lobes will not be air-containing in some portions. The lungs were normal in appearance except for their distention.

Microscopically: There was congestion of the blood vessels and an occasional desquamated epithelial cell and polymorphonuclear leucocyte in the alveoli.

Pn-52. Received 180 c.c. of salt solution and was killed after fifteen minutes. The lungs were similar, both grossly and microscopically, to those of dog Pn-50.

Pn-51. Received 200 c.c. of salt solution and was killed after eighteen hours. Much of the fluid had been absorbed, although there was a considerable amount in the lower lobes.

Microscopically: The picture was practically identical with that presented by Pn-50.

Pn-53 and Pn-54. These dogs received 220 and 210 c.c. respectively. Both were killed after four days. During the interval they appeared to be perfectly well. At autopsy the lungs were found to be practically normal, with but little fluid remaining. The only gross change was the presence of a few pin-point hemorrhagic areas scattered over the surface of the lower lobes.

Microscopically: Some of the bronchi contained a little mucus with a few red blood cells and an occasional polymorphonuclear leucocyte. The picture suggested desquamation of the bronchial epithelium. There was very little inflammatory reaction.

Pn-55. Received 205 c.c. of salt solution. The dog remained apparently normal for ten days, at which time it was killed for examination. The lungs appeared normal, presenting no gross lesions. There was no fluid remaining in any of the lobes. Microscopically, the tissue appeared normal.

The above experiments indicate that a considerable period of time may be necessary before fluid introduced into the alveoli of the lung is entirely absorbed. After eighteen hours much has disappeared and within four days it has been absorbed without a trace. In the interim, however, and for several hours after the insufflation, if the animal is sacrificed a degree of artificial edema may be encountered which is frequently greater than that met with when death is ascribed to this condition. This has led to a consideration of pulmonary edema as a cause of death.

Pulmonary Edema as a Cause of Death. During the past two years, while the studies on the effect of pulmonary irritating gases (2) have been in progress in this laboratory, particular attention has been paid to the very striking phenomenon of pulmonary edema in the gassed subject. The result of these investigations may be briefly summarized in the following paragraphs (3).

Animals which die acutely from exposure to any of the gases of the respiratory irritant group, such as chlorine and phosgene, show at autopsy varying degrees of edema of the lungs. Although this is regularly well marked in certain species, dogs, for example, there are wide individual variations. In other species, rats and guinea pigs, for example, it may be a relatively inconspicuous feature in spite of the fact that these animals are particularly susceptible to effect of the gas.

Dogs which have been killed before the action of the gas reaches its maximum effect likewise show striking differences in the amount

of fluid in the lungs, and these differences do not harmonize with the variations in the symptoms manifested by the animals. Furthermore, many dogs which pass successfully the critical forty-eight hour period and are classed as "recovered" often show, when killed, edema of the lungs of greater degree than other dogs of the same experiment which succumbed.

These observations, together with the results of the experiments previously quoted, upon what may be termed artificial pulmonary edema produced by filling the lungs of a normal dog with isotonic salt solution, have led to the conclusion that edema of the lungs in general is merely an indicator of some underlying disorder, and is not directly responsible for the death of the patient or animal.

Pulmonary Irrigation. It will be recalled that the primary object of this investigation was to determine whether therapeutic agents could be applied directly by the intratracheal route to pulmonary lesions. It has been shown not only that the lung tissue is not susceptible, as is generally believed, to the introduction of foreign material through the trachea, but that large quantities of isotonic salt solution can be introduced without any harmful effects. In fact, artificial edema can be produced which exceeds the grade which is frequently found where death is attributed to this phenomenon, and still the animal shows no untoward symptoms. The question now arises in what way these facts can be utilized for the elaboration of the primary object. It is at once obvious that there are two separate modes of attack: the first, irrigation of the lung tissue through the intratracheal route, and the second, direct application of specific or non-specific chemical or biological agents.

The first of these methods has been more completely investigated, since it seemed possible that it could be utilized successfully in animals during the very acute period after exposure to pulmonary irritating gases. These poisons act upon the respiratory epithelium in such a way as to incapacitate more or less completely the protective mechanism of the upper respiratory tract, and allow, as a consequence, an invasion into the lung of the bacteria from the mouth or from the inspired air (4). The initial damage to the lung already present when the organisms reach it makes this a favorable medium for bacterial growth. Naturally, if the necrotic material with the bacteria could be washed out, beneficial results might be

expected, and for this reason attention was concentrated upon an efficient method of intratracheal irrigation.

The procedure does not differ in any essential way from that described for pulmonary insufflation except that much larger quantities of fluid have been used. The irrigation has been conducted either as a continuous or intermittent process, with the fluid always introduced by the gravity method. In the intermittent method the lungs are entirely flooded with the salt solution, and then the flow from the reservoir is cut off for a few minutes, during which time the lungs are allowed to drain. When the salt solution ceases to flow from the trachea and mouth, the lungs are again flooded, and this process is repeated throughout the application of the perfusion. With the continuous method of perfusion, the force of the flow from the reservoir is cut down and a small stream of fluid is allowed to enter into the lungs throughout the experiment. The intermittent method has given more satisfactory results. It is better tolerated by the animal and there is no serious interference with the respiration. With the completion of irrigation, recovery from the anesthesia occurs somewhat slowly, but in a short time the animal appears normal. The period of irrigation has frequently exceeded three hours and as much as 6000 c.c. of fluid have been allowed to pass through the lungs. It will be unnecessary to include a protocol here, for the method has been utilized to determine the efficiency of the irrigation process after the introduction into the lungs of different substances, including coloring matters, non-pathogenic and pathogenic bacteria. The protocols that follow indicate the efficiency of the method.

Pn-61. June 16, 1918. An insufflation of 20 c.c. of a dilute solution of starch paste was followed by a continuous perfusion for twenty-five minutes of 3000 c.c. of salt solution. Throughout the experiment the effluent continued to give a positive iodine-starch reaction. At the end of the perfusion the dog was killed. The lungs were removed and after the different lobes had been cut with several incisions at different levels, they were tested for the iodine reaction. A positive reaction was secured with the lower right lobe. The starch was uneven in its distribution. All of the larger bronchi and the majority of the smaller ones were free of starch.

Pn-62. June 16, 1918. The above experiment with Pn-61 was controlled by injecting Pn-62 with the same amount of starch paste and testing the lungs in the same manner without the perfusion. The lower right

lobe was full of starch, as was also a portion of the adjacent upper lobe. All of the bronchi from the large ones to those microscopic in size were filled with the paste.

Pn-99. Insufflation of 15 c.c. of a very heavy twenty-four-hour broth culture of *B. prodigiosus*. The tracheal cannula was removed and sterilized. Saline perfusion of the lung to the amount of 3000 c.c., lasting forty-five minutes, was started about twenty minutes after the introduction of the culture. The perfusion was by the intermittent method. At intervals during the perfusion samples were taken from the effluent. These were plated in dilutions for the bacterial count of *B. prodigiosus*.

Samples after Perfusion of	Count per Cubic Centimeter
300 c.c.	2,075,000
600 c.c.	970,000
1000 c.c.	260,000
2000 c.c.	90,000
3000 c.c.	80,000

These two experiments demonstrate conclusively that inert foreign material can be washed out by the method of intratracheal pulmonary irrigation, but even after prolonged treatment of this kind, in which many liters of irrigating fluid are employed, there still remains a residue of the original material introduced.

The experiment with *B. prodigiosus*, in which 96 per cent of the organisms were recovered in the effluent, was most encouraging, and led to the further experiment in which a virulent organism was employed as a measure of the efficiency of the treatment. The culture selected was a pneumococcus Type I, which, when grown in broth for eighteen hours, possessed such virulence that 0.000001 c.c. was uniformly fatal for mice within forty-eight hours. Throughout the experiment this culture was maintained by animal passage at this virulence, and all insufflations were made with eighteen-hour broth cultures. Preliminary experiments showed that 20 c.c. were required to produce a fatal pneumonia when insufflated by the intratracheal route into the lung of a dog, and although the animal became ill, death never followed when even as much as 15 c.c. of this culture was utilized. These preliminary experiments were followed by another group, in which first lethal and then sublethal quantities of culture were insufflated and followed by irrigation. Despite the fact that over 75 per cent of the organisms introduced

were recovered in the effluent by actual count, the animals invariably succumbed with a diffuse pneumonia involving many lobes.

A typical protocol in which a sublethal quantity of culture was utilized is appended.

Pn-VI. January 27, 1919. Ten cubic centimeters of a culture of pneumococcus Type I were introduced by intratracheal insufflation at 9.50 A.M. This was immediately followed by an intermittent intrapulmonary irrigation with 6000 c.c. of salt solution. The dog recovered from the treatment, but grew more and more prostrate and appeared very sick at 9.30 P.M. He survived the night, but died at 10.35 A.M., January 28, 1919.

Blood for culture was taken after the irrigation as follows:

Blood Taken at	Interval Since Insufflation	Plate Count per c.c.
2.15 P.M.	4 hours	no growth
4.30 P.M.	6½ hours	6
7.00 P.M.	10 hours	332
9.30 P.M.	12 hours	850
10.40 A.M. January 28, 1919	(post-mortem)	infinity

The effluent was collected at different stages during the irrigation and each specimen was plated. The individual counts for each sample multiplied by the volumes give the following figures as indicating the number of organisms washed out:

Sample A,	233,450 per c.c.	Total number, 198,432,500
Sample B,	242,200 per c.c.	Total number, 448,070,000
Sample C,	94,000 per c.c.	Total number, 136,300,000
Sample D,	104,000 per c.c.	Total number, 33,280,000
		816,082,500

This figure (816,082,500), when compared with the number of organisms introduced (1,072,000,000), shows that during the irrigation 76 per cent of the organisms were eliminated from the lung.

Needless to say, the result of the experiments with virulent organisms in such sharp contrast to those with saprophytic bacteria was unexpected and has led to considerable speculation. It will be seen that one-half, and in other tests a much smaller number of organisms than represent a minimal lethal dose, a quantity which would cause the animal no inconvenience if their introduction into the lung was not followed by the irrigation procedure, results in a very diffuse and fulminating lobar consolidation.

Several possibilities suggest themselves: that the irrigation damages the lung to a sufficient extent to allow the few bacteria that remain to develop rapidly; that the bacteria multiply even during the short time that the irrigation is proceeding, and, finally, that the flow of fluid through the lung drives some of the organisms so deep into the alveoli that they become more firmly lodged and rapidly multiply. Probably all these factors play a rôle. The rapid development of the septicemia is in favor of pulmonary damage as well as mechanical washing of the organisms into the deeper tissues of the lung. It is, however, not our purpose to discuss this phase of the question.

The experiment quoted above is absolute evidence that irrigation of the lung with salt solution not only cannot be utilized to advantage, but is actually a disseminator and an aggravator of the inflammatory process within the lung.

The above experiments indicate conclusively that a mechanical removal by the irrigation process is inadequate, and immediately suggests the use of very dilute chemical disinfectants or specific or non-specific biological agents.

A number of experiments have been conducted in which chemical disinfectants were used as irrigating substances, but these so far have resulted in the production of pneumonias which are analogous to those that have since been reported by Wollstein and Meltzer (5) and which are designated by them as *chemical pneumonia*. It is hoped that a disinfecting agent may be used sufficiently dilute to be effective and yet not harmful, and that other specific or non-specific biological agents may be found that will render this new route of pulmonary therapy effective.

BIBLIOGRAPHY

1. Wollstein and Meltzer, *J. Exper. M.*, 1918, XXVIII, 551.
2. "Collected Studies on the Pathology of War Gas Poisoning," Yale Univ. Press (in press).
3. Winternitz and Lambert, *J. Exper M.*, 1919.
4. Winternitz, *Mil. Surgeon*, May, 1919.
5. Wollstein and Meltzer, *J. Exper. M.*, 1918, XXVIII, 547.

ENVOI

SIR WILLIAM OSLER AND THE AMERICAN MEDICAL OFFICER

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ALL England abounded in hospitality for the American cousin during the summer of 1918. My duties placed me there, and I saw that the spirit of welcome made no specifications of rank. To the medical officer, the great centers of medical thought and teaching in London, Leeds, and other cities held forth the unending invitation, but there remained one host embodying within himself a whole medical center, and Sir William Osler furnished the attraction and the recompense.

The door of the lovely home at Oxford had no latchstring—it was simply perennially open to the American medical officer stationed in England, or transiently stopping there.

There was motive a plenty in going to Oxford to see the leader, but a newer and a stronger impulse to go again came to him who went once, in the welcome which he found and the inspiration and uplift he carried away. It was the easier to love one's kind, and make the necessary sacrifice for them, when one had sat in the warm glow of the fine spirit, which enveloped the listener, with the amiable and instructive counsel and good fellowship of his kindly heart and keen mind.

It was a rare privilege to be able to go to Oxford as Oxford, but to go there and be met by the living sage, to induct one into the atmosphere of the sages gone before, was to do a thing marking a red-letter day.

But the gentle sage did not rest satisfied that he should do no seeking, and straightway he came to all our hospitals, whether to speak to a local clinical meeting, to raise an American flag, or look over the state of our sick, and I doubt that he will ever in any degree realize the response his inspiriting presence evoked in the

hearts of the elders and the youngsters who sat in his presence. Who of those men were not his disciples, for who had not read the fascinating pages of his cornerstone of modern medical practice?

Our good Sir William—for we Americans cannot forego our partnership in him—lent all that was at his command to the advancement of American interests in England, and how he helped us is a grateful and a delightful recollection to those of us whose military fortunes were cast in the mother country during the period of the war. The whole world of medicine lays its tribute at his feet, and from no element in that broad concourse is the tribute more instinct with love and admiration than in the little offering made by us of the A. E. F. in England.

[THE END]